INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE ROSUVASTATIN TABLETS: A COMPARATIVE STUDY ON NATURAL AND SYNTHETIC SUPER DISINTEGRENTS

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Article Received on: 04/05/16 Revised on: 25/05/16 Approved for publication: 29/05/16

DOI: 10.7897/2230-8407.07660

ABSTRACT

The delivery of drugs to the oral cavity, for local action or, in some cases, absorption across the oral mucosa, thereby avoiding first-pass hepatic metabolism and potentially increasing the rate and extent of uptake, and reducing undesirable metabolites these ODT's plays a predominant role. The objectives of the research work was to formulate Rosuvastatin oral disintegrating tablet by using natural and synthetic superdisintegrents. in different ratio by direct compression technique and tablets were evaluated for precompressional and postcompressional Parameters such as angle of repose, bulk density, tapped density, compressability index, drug content and in-vitro drug release study, hardness, friability, wetting time and invitro dispersion time. To study the physical characteristics of the individual drug and optimized formulations by FTIR spectroscopy. To evaluate various characteristics of the resulting tablets. Formulation F3 was shown good releasing characteristics when compared all the super disintegrents.

Key words: Rosuvastatin, Crospovidone, cross carmellose sodium, Crospovidone, sodium starch glycollate

INTRODUCTION

Oral disintegration tablets are the novel technology for administration of the drug through the oral route. ODT's are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Many patients find it difficult to swallow like pediatric and geriatric and those people who are travelling or little access to water and some patients who are mentally ill like schizophrenia they are also did not take medicine, oral disintegrating tablets solve these problems. An Oral disintegration tablets is a solid dosage form that disintegrates and dissolves in the mouth without water within 60 seconds or less. orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Additionally, pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control[1,2].

Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that Dysphagia[3] (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue[4]." ODT products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia).

MATERIALS AND METHODS

Extraction of *Ocimum bacilicum* seeds mucilage

The Ocimum seeds were kept in contact with petroleum ether in a stoppered conical flask for 12 h. The flask was kept on the electrical shaker for the continuous shaking. The material was then filtered out and dried at room temperature for complete removal of petroleum ether. The seeds were then soaked in distilled water for overnight. The swollen seeds were subjected to agitation by using mechanical stirrer (Remi electrotechnik Ltd.) with 1000 RPM for 2hrs. The agitated mass of seeds were then passed through the 8 folds of the muslin cloth. The filtrate was then precipitated in 3 volumes of acetone then spread on a glass tray and air dried. The dried material was then passed through mesh #30. The material was winnowed and again passed through mesh #60. The weight of mucilage obtained was recorded.

Preparation of Mixed blends of drug and excipients

Rosuvastatin and all the ingredients were weighed accordingly specified in the formulation (table.no.1) and mixed by means of geometrical dilution for about 15min to make uniform blend. Magnesium Stearate and Talc both have passed through sieve #60 separately and mixed with the above blend for sufficient time usually 5-7 min. To the mixed blend of powder and excipients finally add magnesium stearate. The mixed blend was compressed with sixteen (16) station tablet punching machine using 7 mm flat punches with break line. Four punches in the twelve station compressor are fixed with die cavity and remaining is fixed with dummy punches.

Evaluation of Precompressional Parameters of Oro Dispersible Tablets Blend[9]

Bulk density: Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume(V_b) and weight of the powder was determined.

$$\text{Bulk density} = M / V_b$$

Tapped density: The measuring cylinder containing a known mass of powder blend was tapped for a fixed number of times as per USP apparatus-II. The minimum volume occupied by the powder after tapping was measured.

Tapped density = weight/tapped volume

Compressibility index; Compressibility index is calculated as follows.

Tapped density- Bulk density/ Tapped density*100

The value below 15% indicates a powder with good flow characteristics where as above 25% indicates poor flowability.

Haussner's ratio; It is an indirect index of ease of powder flow, it is calculated as follows.

Tapped density / Bulk density

Haussner's ratio <1.25 indicates good flow properties, where as >1.5 indicates poor flowability.

Angle of Repose; Angle of repose was determined using funnel method. The blend was poured through funnel that can rise vertically until a maximum cone height (h) was obtained. Radius of the heap(r) was measured and angle of repose was calculated as follows. The results were shown in Table 2.

$$\theta = \tan \quad h/r$$

Carr's index (I)
It helps in measuring the force required to break the friction between the particles and the hopper. Results are showed in table no 7.5. It is expressed in % and given by:

$$= \frac{-}{} \quad 10$$

Where,
Dt = The tapped density, Db = The bulk density.
Application:- It is indirectly related to powder flow, property and cohesiveness.

Evaluation of Post-compressional parameters of Rosuvastatin Oral Disintegrating tablets[10]

All the prepared tablets were evaluated for the following parameters as per the I.P guidelines and the results are given in the table7.

Weight variation
Twenty tablets from each formulation were selected randomly and average weight was determined. Individual tablets were then weighed and compared with average weight.

Hardness test
The force required to break a tablet in a diametric compression was determined by using Pfizer tablet hardness tester.

Friability
The weight of twenty tablets was noted and placed in the friabilator and then subjected to100 revolutions at 25 rpm. Tablets were dedusted using a soft muslin cloth and reweighed.

Percent friability = [initial weight – final weight / initial weight] × 100

Wetting time and Water absorption ratio
A piece of paper folded twice was kept in a petri dish (internal diameter 6cms) containing 6ml of purified water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was weighed. Water absorption ratio, R was determined using the following equation.

$$R = [Wa – Wb / Wb] \times 100$$

where Wa, Wb are the weights of tablets before and after wetting.

In vitro dispersion time
Tablet was added to 10ml of distilled water at 37± 0.5˚C, time required for complete dispersion of tablet was measured.

Drug content uniformity
The drug content uniformity was determined by taking the powder equivalent to 10mg, then it was (n=3) dissolved in P^H6.8 phosphate. Required dilution (10µg/ml) was prepared and absorbance was taken against the blank at 206nm.

In vitro disintegration time
The disintegration was performed using an I.P 85 disintegration apparatus with distilled water at 37±0.5 ˚C.

Dissolution studies
Dissolution rate of Rosuvastatin from all formulations was performed using LABINDIA DISSO 2000 an eight stage dissolution rate testing apparatus with paddle. The dissolution fluid was 900 ml of P^H6.8 phosphate buffer with a speed of 50 rpm and temperature of 37±0.5˚C were used in each test. 5 ml of sample was withdrawn at different time intervals (2.5, 5, 10, 15 & 20 mins) and fresh medium was replaced to maintain sink conditions. The samples are analyzed by using UV- Visible spectrophotometer at λ_{max} 241 nm. Dissolution studies were performed in triplicate.

Stability Studies
Stability testing is an integral part of formulation development. It generates information on which to base proposals for the shelf lives of drug substances and products and their recommended storage conditions. Stability data also are a part of the dossier submission to regulatory agencies for licensing approval.
Stability testing ensures that a drug substance will be safe and effective throughout the shelf life of the product. However, meeting the potency and purity profiles established in the compendia can be challenging as pharmaceutical products become increasingly complex and diverse.
The optimized formulation F6 packed in PVC blister pack then, they were stored at three different temperatures $4^0C±2^0C$, $27^0C±2^0C$ and $45^0C±2^0C$ for 45 days at RH 75±5%. At 15 days intervals, the tablets were evaluated for their physical appearance, drug content and drug excipients compatibility at specified intervals of time.

Table 1: Formulation of oral disintegrating tablets of Rosuvastatin by using natural and synthetic superdisintegrants

Ingredients (mg per tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Rosuvastatin	10	10	10	10	10	10	10	10	10	10	10	10
Lactose Anhydrous	81.5	79	74	81.5	79	74	81.5	79	74	81.5	79	74
CrosCarmellose Sodium	2.5	5	10	---	---	---	---	---	---	---	---	---
Sodium Starch Glycolate	---	----	---	2.5	5	10	---	---	---	---	---	---
CrossPovidone	---	---	---	---	---	---	2.5	5	10	---	---	---
Ocimum Bacilum Mucilage	---	---	---	---	---	---	---	---	---	2.5	5	10
Acesulfame Potassium	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total Weight	100	100	100	100	100	100	100	100	100	100	100	100

* All Weights are represented in mg.

Table 1.2: Evaluation of Pre-Compression Parameters

Formulation code	Evaluation of precompression parameters					
	Bulk density* (g/ml)	Tapped density (g/ml)	Compressability Index	Carr's index (%)	Hausner's ratio	Angle of repose ($^{\theta}$)
F1	0.422±0.2	0.478	17.2	20.12	1.22	26.54
F2	0.44±0.2	0.493	16.8	18.24	1.20	25.68
F3	0.432±0.4	0.524	15.6	19.54	1.22	24.52
F4	0.468±0.2	0.532	18.6	18.44	1.24	26..88
F5	0.478±0.6	0.528	18.2	20.86	1.22	28.64
F6	0.426±0.2	0.546	16.6	16.44	1.26	24.82
F7	0.478±0.8	0.516	16.4	20.44	1.22	28.96
F8	0.410±0.6	0.542	15.8	19.84	1.23	26.86
F9	0.402±0.6	0.538	14.6	14.24	1.21	23.68
F10	0.454±0.4	0.572	15.8	20.48	1.18	29.47
F11	0.498±0.4	0.556	15.2	19.44	1.22	27.63
F12	0.436±0.4	0.548	14.8	15.86	1.20	23.48

Table 1.3: Quality control tests for the oral disintegrating tablets of Rosuvastatin

Formulations*	Avarage Weight*	Hardness *Kg/cm^2	Friability *(%)	Wetting time*	Water absorption ratio*
F1	99.2±0.12	3.8±0.11	0.58±0.16	22.12±0.21	41±0.14
F2	99.6±0.21	3.7±0.24	0.56±0.17	20.13±0.34	39±0.15
F3	98.3±0.16	3.6±0.44	0.57±0.18	19.11±0.16	40±0.24
F4	99.5±0.25	3.8±0.11	0.56±0.16	18.87±0.16	44±0.16
F5	98.9±0.54	3.9±0.14	0.48±0.19	26.76±0.19	42±0.14
F6	99.3±0.01	3.9±0.17	0.50±0.24	22.41±0.13	40±0.18
F7	98.5±0.19	3.8±0.21	0.52±0.21	24.13±0.77	48±0.19
F8	99.1±0.71	3.7±0.15	0.56±0.27	21.14±0.14	42±0.28
F9	**99.9±1.8**	**3.5±0.49**	**0.57±0.17**	**15.55±0.15**	**38±0.14**
F10	97.7±0.16	3.6±0.2	0.54±0.16	19.12±0.13	40±0.13
F11	98.8±0.87	3.6±0.32	0.59±0.22	17.56±0.12	38±0.17
F12	**99.8±0.321**	**3.5±0.225**	**0.58±0.28**	**15.02±0.196**	**34±0.224**

* Data represent mean ±SD (n=3)

Table 1.4: Quality control tests for the oral disintegrating tablets of Rosuvastatin

Formulations*	Disintegration time * (sec)	Drug content* (%)	Percentage Drug Dissolved After 10 min*.	In vitro Dispertion time* (s)
F1	48.55±0.45	99.21±0.73	79.24±0.42	25±0.22
F2	46.51±0.71	99.97±0.12	82.21±0.31	23±0.65
F3	38.44±0.61	98.58±0.53	88.24±0.86	21±0.72
F4	55.21±0.14	99.25±0.62	80.24±0.68	31±0.25
F5	51.85±0.32	98.21±0.54	86.25±0.45	29±0.36
F6	50.21±0.68	99.56±0.41	89.35±0.76	26±0.62
F7	49.25±0.21	98.95±0.25	76.91±0.13	30±0.98
F8	48.65±0.24	99.78±0.61	82.24±0.95	24±0.57
F9	**32.78±0.32**	**99.9±0.32**	**92.42±0.42**	**18±0.24**
F10	48.24±0.45	97.25±0.23	81.21±0.68	24±0.57
F11	40.24±0.55	98.6±0.4	86.21±0.9	22±0.32
F12	**32.9±0.986**	**99.7±0.56**	**92.9±0.64**	**19±2.44**

* Data represent mean ±SD (n=3)

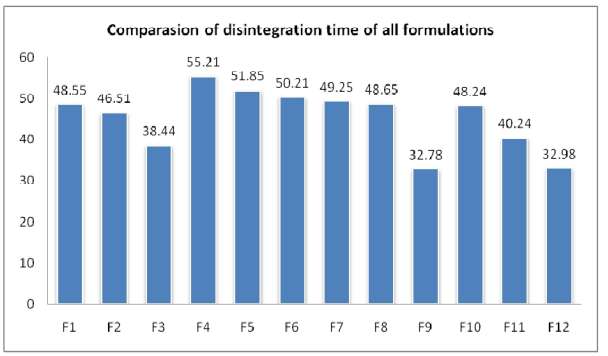

Figure 1: **Comparison of disintegration time of all formulations**

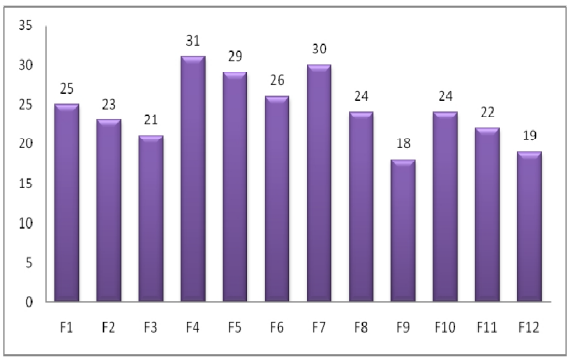

Figure 2: Comparison of In vitro Dispersion time of all formulations

Table 1.5: Dissolution profile of the oral disintegrating tablets of Rosuvastatin

Formulations	Cumulative % drug dissolved (mins)						
	0	2.5	5	10	15	20	25
F1	0	48.6±0.26	59.24±0.35	69.24±0.42	80.25±0.24	89.47±0.31	96.21±0.73
F2	0	55.25±0.12	62.25±0.95	82.21±0.31	89.350.89	94.28±0.71	97.97±0.12
F3	0	49.24±0.21	60.26±0.31	73.24±0.86	81.78±0.21	92.12±0.11	98.58±0.53
F4	0	54.2±3.16	61.21±0.24	72.24±0.68	80.9±0.1	88.24±0.21	96.25±0.62
F5	0	53.21±0.14	60.21±0.1	74.25±0.45	82.7±0.31	91.25±0.14	98.21±0.54
F6	0	55.8±2.3	66.35±0.35	74.35±0.76	81.36±0.32	89.27±0.12	98.56±0.41
F7	0	53.8±1.26	67.2±0.54	76.91±0.13	84.4±0.12	91.14±0.78	96.95±0.25
F8	0	45.6±0.51	60.5±0.32	72.24±0.95	80.6±0.85	89.7±0.74	97.78±0.61
F9	**0**	**56.75±2.5**	**69.35±0.12**	**78.42±0.42**	**86.25±0.2**	**93.26±0.32**	**99.79±0.32**
F10	0	50.26±0.2	62.24±0.21	74.21±0.68	81.19±0.2	88.02±0.13	96.25±0.23
F11	0	51.12±0.74	60.26±0.1	70.21±0.9	78.42±0.6	89.27±0.1	97.26±0.4
F12	**0**	**55.46±5.46**	**67.88±0.31**	**75.9±0.64**	**83.26±0.11**	**91.56±0.26**	**99.64±0.56**

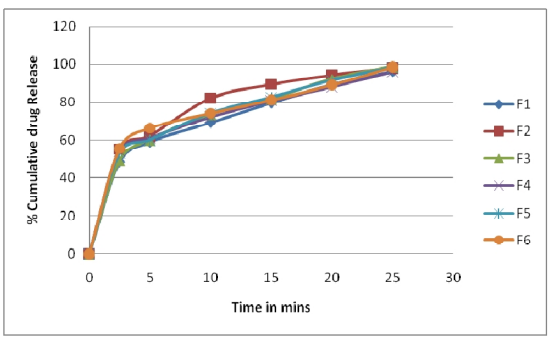

Figure 3: % Cumulative drug release for formulations F1-F6

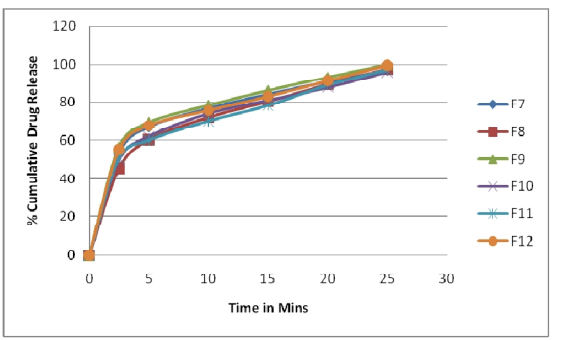

Figure 4: % Cumulative drug release for formulations F7-F12

RESULTS AND DISCUSSIONS

The first 9 formulations of Rosuvastatin calcium were formulated with different Concentrations (2.5%, 5% and 10%) of synthetic super disintegrants namely, croscarmellose sodium, sodium starch glycollate and crospovidone. Lactose was used as diluents, Magnesium stearate and talc are used as lubricants and glidant respectively.The F10 to F12 formulations are formulated using Ocimum bacilum as a superdisintegrant in different concentrations (2.5%, 5% and 10%).FTIR studies reveled that there is no drug –excipients interaction as all the characteristic peaks of drug were appeared in the formulations (-NH- 3274.34, C=O in esters 1751.36, C=O in acids 1727.03, C=O in amides 1647.59).

For each formulation blend of drug and excipients were prepared and evaluated for various pre compressional parameters like angle of repose, bulk density, tapped density, carr's index and hausner's ratio. The powder blend of all the formulations had hausner's ratio of 1.18 indicating good flowability. The carr;s index was found to be between 14.24-20.86% indicating fairly good flowability of the blend. The good flowabiliy of blend was also made evident with angle of repose values which is below 40° indicating good flowability. Since the powder material was free flowing , tablets were prepared by direct compression technique.

The drug content was found to be in the range of 97.25- 99.9 (within the acceptable limit) and the hardness of the tablets between 3.5-3.9 Kg./cm^2. The wetting time of the formulations was found to be 15.02-26.76 sec. and the disintegration time was ranging from 32.78 to 55.21 seconds. The wetting time and disintegration time both are less for the formulation containing crospovidone (10%w/w) as super disintegrant. The formulation with crospovidone shows faster disintegration and wetting time than formulation with ocimum bacilicum and other synthetic super disintegrants. The order of enhancement of dissolution rate with various super disintegrants was found to be crosspovidone > Ocimum Bacilicum > sodium starch glycollate > Croscarmalose sodium. The dissolution profile, wetting time

of optimized formulations were compared.The dissolution profile wetting time and disintegration time of optimized formulations were compared with the marketed conventional tablets Rosuvastatin. Drug released from conventional tablets were more when compared with the tablets manufacture with the crospovidone and ocimum bacilum. The stability studies for the optimized formulations F9 and F12 were performed for about 2 months at 40˚C / 75% RH AND 25˚C /60%RH. The samples were analyzed at intervals of 0, 15,30, 45 and 60 days. There were no significant change in the physical appearance of the tablets, disintegration time and wetting time .

SUMMARY

The aim of the present study was to develop and optimize oral disintegrating tablets of drug (Rosuvastatin) to give quick onset of action by rapidly disintegrating in a few seconds without the need of water with better patient compliance. In such cases, bioavailability of drug is significantly greater and adverse event is reduced than those observed from conventional tablet dosage form. By performing compatibility studies by IR spectrophotometry, no interaction was confirmed. Oral disintegrating tablets were formulated by direct compression method and evaluated by UV-Visibile spectrophotometer. Standard calibration curve prepared to determine the drug content in the prepared tablets. Prior to compression, the blend of drug and excipients were evaluated for flow properties such as Angle of repose, Bulk density, Tapped density, % Compressibility, and Hausner ratio. All the formulation showed good flow properties. Oral disintegrating tablets were prepared by direct compression technique using CADMACH 16 station tablet punching machine, equipped with round flat punches of 8 mm diameter. Post compression evaluation of prepared oral disintegrating tablets were carried out with the help of different pharmacopoeial and non-pharmacopoeial (industry specified) tests. The shape and color of all the formulations were found to be circular and white in color. The thickness was found to be uniform in specific formulations. The hardness and friability are also within the permitted limits. Dissolution of tablets was carried out. The crospovidone and Ocimum bacilicum used formulations gave the more dissolution profile compared to other synthetic superdisintegrants.

CONCLUSION

The above results suggest that the formulated oral disintegrating tablets of Rosuvastatin exhibited good physical parameters and rapidly disintegrating without affecting the release profile and is very effective in case of elderly and pediatric patients. The overall results indicated that formulation with crospovidone (10%) and ocimum bacilicum had a higher edge compared to other formulations containing synthetic superdisintegrants. They satisfy all the criteria for oral disintegrating tablets. This direct compression process is simple, reproducible and robust to prepare orally disintegrating tablets Rosuvastatin.

ACKNOWLEDGEMENT

The author was very thankful to principal and the management of Gurram Balanarasaiah Institute of Pharmacy for providing all the necessary facilities and given continuous encouragement throughout the research work.

REFERENCES

1. SeagerH, Drug delivery products and the zydus fast dissolving dosage forms, J.Pharm.Pharmacol. 1998, 50(4), 375-382.
2. Indurwade, N. H., Rajyaguru,T. H. and Nakhat, P.D., Fast Dissolving drug delivery systems: A Brief overview, Indian Drugs, 2002, 39(8), 405-09.
3. Devrajan,P.V,Gore, S.P., Fast Dissolving Tablets: The Future Compaction, Express Pharma Pulse, 2000: 23, 7(1), 16.
4. Habib W, Khankari R, Hontz J., "Fast-dissolving Drug Delivery Systems", Critical Reviews ™ Therapeutic Drug Carrier Systems**,** 2000, 17(1), 61-72.
5. Rowe.R.C, shestey P.J, Weller P.J Hand book of pharmaceutical excipients, 6th edition, london, Chicago:Pharmaceutical press, American pharmaceutical association;2009.
6. www.drugbank.ca
7. Rajeshree Panigrahi1, K.A.Chowdary, Gitanjali Mishra, Manas Bhowmik, Effect of Combination of Natural Superdisintegrants on FastDissolving Tablets of Lisinopril, International Journal of Pharmaceutical Research and allied sciences, ISSN 2277-3657, Volume 1, issue 3 (2012), 73-78.
8. Sunada, H., Bi Y., Preparation, evaluation andoptimization of rapidly disintegrating tablets, Powder Technol., 2002, 122(23), 188-198.
9. Goyani Sandip, M, Shah Pranav, Vyas Bhavin, Shah D.R, Formulation and evalution of Orally disintegrating tablets of Meclizine hydrochloride, Int Res J Pharm, 2012;3(3):196-199
10. Brahmaiah Bonthagarala, Prasanth Pasumarthi, Katta Vamsi Kiran, Sathram Nataraja, Sudarshan Donthiboina. Formulation and evaluation of orodispersible atenolol maleate tablets: A comparative study on natural super disintegrents and synthetic super disintegrents. Int. J. Res. Ayurveda Pharm. 2014;5(2):185-192 http://dx.doi.org /10.7897/2277-4343.05237

Cite this article as:

Rajeshwar V, M. Venkata Ramana. Formulation and evaluation of orodispersible rosuvastatin tablets: A comparative study on natural and synthetic super disintegrents. Int. Res. J. Pharm. 2016;7(6):39-43 http://dx.doi.org/10.7897/2230-8407.07660

Source of support: Nil, Conflict of interest: None Declared