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Formulation and Evaluation of Rosuvastatin Immediate Release Tablets 10 Mg

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Abstract: *Rosuvastatin is a member of the drug class statins, used to treat high cholesterol and to prevent cardiovascular disease. It comes under class II of Biopharmaceutical Classification System. The objective of present study is to develop Rosuvastatin immediate release tablets 10 mg using different types of superdisintegrants to enhance the disintegration time and dissolution of Rosuvastatin calcium to improve bioavailability of the drug. In the present study immediate release formulation of Rosuvastatin calcium was prepared by wet granulation method that are cost effective. Different formulations were made by using various concentrations of superdisintegrants such as Crospovidone, Sodium Starch Glycolate and Kyron T-314 (Polacrillin Potassium). The Prepared formulations were evaluated for the physical characteristics, in vitro dissolution and stability at 40°C/ 75% RH for six months. Among all the formulations F2 (containing 4.5% of super disintegrants i.e., crospovidone) was considered to be the best formulation, which releases up to 102.4% drug in 30 minutes. From this study we can conclude that, formulated tablets of Rosuvastatin containing crospovidone are better and effective than conventional tablets to meet patient compliance.*

Keywords – *Rosuvastatin Calcium, Superdisintegrants, Crospovidone, Sodium Starch Glycolate, Kyron T-314, Patient Compliance.*

I. Introduction

The need for new oral drug delivery system continues, due to poor patient acceptance for invasive methods, need for exploration of new market for drugs and coupled with high cost of disease management. Developing new drug delivery techniques and utilizing them in product development is critical for Pharma companies to survive this century. Immediate release dosage form is those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. This term excludes formulations which are adapted to provide for "modified", "controlled", "sustained", "prolonged", "extended" or "delayed" release of drug.[1, 2,3]

Immediate release solid oral dosage forms are classified as either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally accomplished in less than one hour. To enhance dissolution and hence bioavailability of any drug from immediate release tablets, disintegration is one of the important process. Few Superdisintegrants are available commercially as Croscarmellose sodium, Crospovidone and SSG.[4,5]

Several Technologies are available to manufacture immediate release tablets. The most common preparation methods are moulding, lyophilisation or freeze drying, direct compression, spray drying and sublimation. Direct compression, is one of the techniques that requires the incorporation of a superdisintegrants into the formulation. Direct compression does not require the use of water or heat during the formulation procedure and is very sensitive to changes in the type and proportion of excipients and the compression forces, when used to achieve tablets of suitable hardness without compromising the rapid disintegration characteristics.[6]

Rosuvastatin, as rosuvastatin calcium is a HMG-CoA reductase inhibitor used for the treatment of dyslipidaemia with absolute bioavailability 20%. [7]

The objective of present study is to develop immediate release tablets of rosuvastatin using different types of super disintegrants to enhance the disintegration time and dissolution of rosuvastatin to improve bioavailability of the drug.

II. Materials and Methods

2.1 Materials

All the chemicals and reagents used in this study were of analytical grade. Rosuvastatin calcium (Cadila Helthcare Ltd, India) was a gift sample from Nuvista Pharmaceuticals Limited, Bangladesh. Other excipients such as Crospovidone (BASF South East Asia Pvt. Ltd.), Sodium Starch Glycolate (Yung zip Chemical Co. Ltd. Taiwan), Kyron T-314 (Corel Pharma Chem, India), Colloidal silicon dioxide (Evonic Resource Efficiency GmbH, Germany), Magnesium stearate (Dr. Paul Lohmann), Microcrystalline cellulose 102 (Mingtai Chemical Taiwan) and Lactose Spray Dried (Foremost Farm, USA) were used. Suitable storage conditions were maintained to store the working chemicals and reagents.

2.2 Formulation of Rosuvastatin immediate release tablets

Weigh all the ingredients accurately according to table 1. Formulas (F1- F4) were prepared by direct compression method in which all constituents were mixed and compressed directly by tablet machine. Mix all the ingredients geometrically except Colloidal silicon dioxide and Magnesium Stearate. Then lubricate the blend with Colloidal silicon dioxide and Magnesium Stearate. The blend was compressed using rotary tablet machine-12 station with 8mm flat punch, B tooling. Each tablet contains 10.42 mg Rosuvastatin calcium equivalent to 10 mg Rosuvastatin and other pharmaceutical ingredients as in Table 1.

Table 1: Composition of different formulas

S. No.	Ingredients	F1	F2	F3	F4
01	Rosuvastatin Calcium	10.42	10.42	10.42	10.42
02	Microcrystalline cellulose 102	75.48	75.48	32.00	75.48
03	Lactose Spray Dried	45.00	45.00	86.40	45.00
04	Crospovidone	-	6.30	4.22	-
05	Sodium Starch Glycolate	6.30	-	4.20	-
06	Kyron T-314	-	-	-	6.30
07	Colloidal silicon dioxide	1.40	1.40	1.38	1.40
08	Magnesium stearate	1.40	1.40	1.38	1.40
09	**Total amount (mg)**	**140.00**	**140.00**	**140.00**	**140.00**

2.3 Evaluation of Tablets [8]

2.3.1 Thickness

The thicknesses of the tablets were determined using a Vernier caliper, 20 tablets from each batch were used and average values were calculated.

2.3.2 Uniformity of weight

Every individual tablet in a batch should be in uniform weight and weight variation in within permissible limits. The weights were determined to within ±1mg by using digital balance. Weight control is based on a sample of 20 tablets.

2.3.3. Percent drug content

For this at least 30 tablets were randomly selected. Out of 30 tablets 10 tablets were crushed into fine powder assayed individually after proper dilution at 242 nm using a UV spectrophotometer.

2.3.4 Hardness and friability

For each formulation, the hardness and friability of 20 tablets each were determined using the hardness tester and friabilator test apparatus, respectively.

2.3.5 Disintegration

The disintegration test is carried out using the disintegration tester which consists of a basket rack holding 6 plastic tubes, open at the top and bottom, the bottom of the tube is covered by a 10-mesh screen. The basket is immersed in a bath of suitable liquid held at 37^{o}C, preferably in a 1L beaker.

2.3.6 In-vitro dissolution study

The dissolution test was performed using USP dissolution testing apparatus 2 (paddle method);
Medium - Phosphate buffer (pH 6.8)
Volume- 900 ml
Temperature- 37^{o}C
RPM – 50
Time intervals- 0, 5, 10, 15 and 30 mins.
Volume of sample replaced- 5ml

Absorbance of these solutions was measured at the wavelength of 242nm by using UV-Visible spectrophotometer.

2.3.6 Accelerated Stability Studies [9]

Rosuvastatin immediate release tablets were evaluated for accelerated stability studies and parameters like hardness, disintegration time, drug content and in vitro drug release were analyzed after storing them at 40±2°C / 75±5% RH for 6 months.

III. Results and Discussion

3.1 Physicochemical evaluation of tablets

Formulations trials from F1 to F4 (Table.No.2 and Figure No. 1 & 2) had thickness with ±5% variation of standard value and hardness was found within the range 80-112 N. Friability was less than 1% which was acceptable. Average weight of all the tablets was around 140±5%. Disintegration time was within the range of 2 -3 minutes. Assay was found within the range 9.7-10.2 mg/tablet. All the formulations satisfied the official compendial requirements.

Table 2: Physicochemical evaluation of various formulations

	Physicochemical evaluation parameters			
Formulation	Hardness *(N)	Friability *(%)	Disintegration time* (minute)	Assay (mg/tablet)
F1	89.2	0.3	3.0	9.7
F2	116.3	0.2	3.0	10.1
F3	105.8	0.4	3.0	9.9
F4	111.9	0.2	2.0	10.2

*All value are express as Mean (n=10)

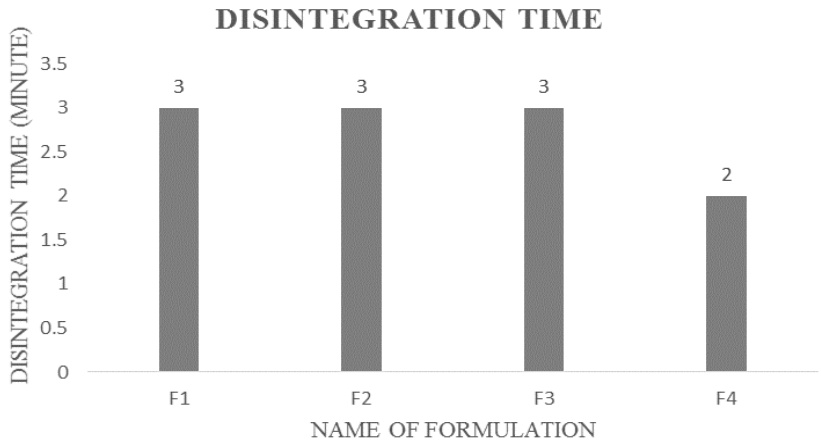

Figure 1: Disintegration Time for different formulations (F1, F2, F3 and F4)

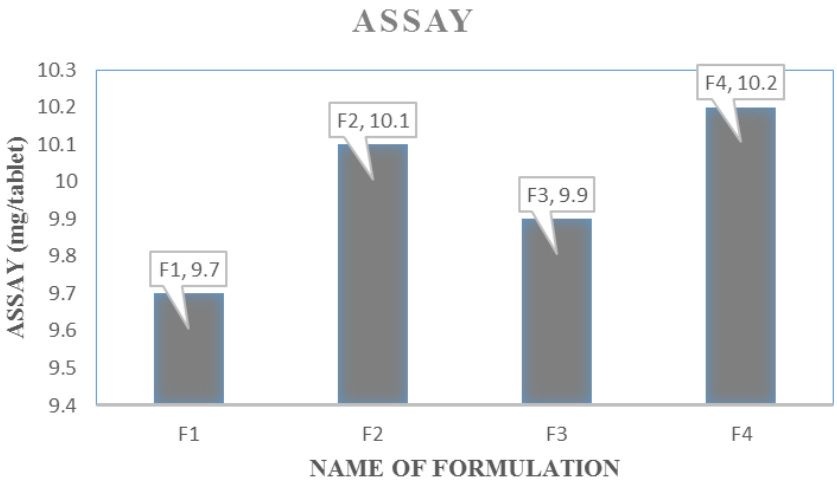

Figure 2: Assay for different formulations (F1, F2, F3 and F4)

3.2 In vitro drug release studies

In –vitro drug release studies (Table.No.3 & Figure.No.3) revealed that 100% drug release was found in 30 min. It was found that formulation F2 have shown best results. So, formulation (F2) was taken as optimized formulation.

Table 3: In vitro drug release evaluation of various formulations

Formulation	Percentage of drug release after 30 minutes*
F1	103.5%
F2	102.4%
F3	96.1%
F4	94.3%
Innovator	98.7%

*All value are express as Mean (n=10)

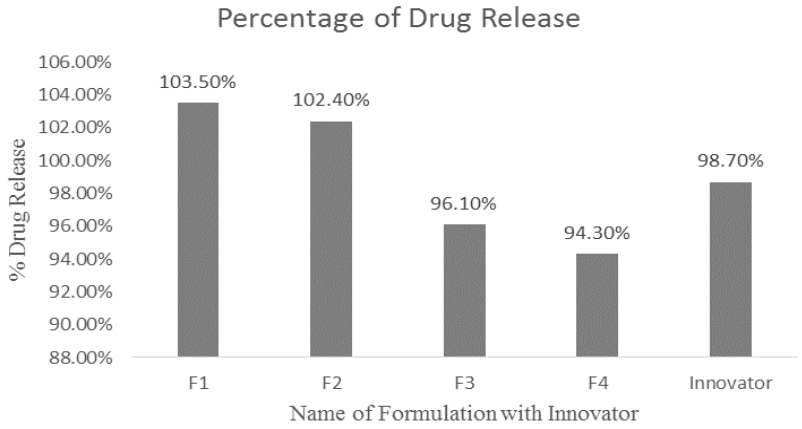

Figure 3: Percentage of Drug Release for different formulations (F1, F2, F3 and F4) and Innovator.

Accelerated stability studies

Accelerated stability studies (Table 8&9) were carried out for a period of 3 months at 45°C/75% RH for F8 formulation. Stability studies for physical appearance, friability, hardness, disintegration time, assay and in vitro drug release were done at different time periods. It was found that there were no changes even after three months of stability study.

Formulation	**Time Period**	**Disintegration Time***	**Assay***	**Dissolution after 30 min.***
F1	**Initial**	3 min	9.7 mg	103.5%
	After 3 months	2 min	9.6 mg	93.9%
	After 6 months	2 min	9.6 mg	94.5%
F2	**Initial**	3 min	10.1 mg	102.4%
	After 3 months	1 min	9.7 mg	99.1%
	After 6 months	3 min	9.6 mg	98.3%
Formulation	**Time Period**	**Disintegration Time***	**Assay***	**Dissolution after 30 min.***
F3	**Initial**	2 min	10.0 mg	100.1%
	After 3 months	3 min	9.7 mg	96.2%
	After 6 months	3 min	9.5 mg	93.4%
F4	**Initial**	2 min	10.0 mg	96.1%
	After 3 months	2 min	9.3 mg	89.6%
	After 6 months	2 min	9.5 mg	94.1%
Innovator	**Initial**	3 min	10.1 mg	101.3%
	After 3 months	2 min	9.9 mg	100.4%
	After 6 months	2 min	9.8 mg	99.1%

*All value are express as Mean (n=10)

IV. Conclusion

In the present work, develop and evaluation of Rosuvastatin immediately release tablet 10 mg using different superdisintegrants. The results of all formulations for weight variation, friability, hardness and drug content were found to be within the limit and no significant variation. Based on the In-vitro dissolution studies, it was found that the drug release for F1 and F2 formulations are comparable to Innovator. But, formulation F3 and F4 showed the significant difference.

Stability study was conducted on formulation of all batches stored at 40ºC/ 75% RH for 6 months and no significance difference was found in results between F2 and Innovator. From the results it may be concluded that formulation F2 may be as an ideal immediate release Rosuvastatin tablets 10 mg by direct compression method. Therefore, long term stability study and clinical trial is required for future development of this formulation.

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