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FORMULATION AND EVALUTATION OF HYDROPHOBICS DRUG ROSUVASTATIN TABLET BY USING THE SOLID DISPERSION METHOD

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Abstract: Solubility enhancement is a difficult task in to the formulation scientist because 80 percent of the drug having the poor boiavaiblity. For the formulation of the dosage form it is necessary to enhance the solubility of the drug. There is various techniques to enhance the solubility of the hydrophobic drugs such as kneading method, hot melt extrusion and solid dispersion. In this research work by using the solid dispersion method to enhance the solubility of rosuvastatin and convert in to the fixed dose of tablet formulation and its evaluation parameters formulation batches are to be design F1,F2,F3,F4,F5. Calibration curve are to be prepared or rosuvastatin pure form and scan at the lambda max 244 λmax. And obtain the r^2 value 0.999 Formulation F5 shows better results and full fill all the parameter compare with the marketed formulation.

Key words: Solid dispersion method, Rosuvastatin tablet, Calibration curve, in vitro release profile.

INTRODUCTION

Now a day's in pharmaceutical industry scientists face the problem of poor aqueous hydrophobic drugs, hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include enhancing solubility and dissolution rate of poorly water-soluble drugs and enhancing permeability of poorly permeable drugs. Enhancing the solubility and dissolution rate of drugs can be increased by a well-known process of fabricating solid dispersions. The enhancements of oral bioavailability of such poorly water-soluble drugs often show poor bioavailability because of low and erratic levels of absorption. Drugs that undergo dissolution rate limited gastrointestinal absorption generally show improved dissolution and bio availability as a result of reduction in particle size. [1] The resulting enhanced surface area produces higher dissolution rate and bioavailability of poorly water soluble drugs. In addition, in solid dispersions, a

portion of drug dissolves immediately to saturate the gastrointestinal tract fluid, and excess drug precipitates as fine colloidal particles or oily globules of submicron size.

Material and Method

Rosuvastatin was a gift sample obtain from the Niksan pharmaceutical and all the polymer which is required in the project work can be used from the central chemical store SPU, Balaghat.

Rosuvastatin

Molecular Formula : $C_{22}H_{28}FN_3O_6S$

IUPAC Name : (*E*,3*R*,5*S*)-7-[4-(4-fluorophenyl)-2-[methyl(methylsulfonyl)amino]-6-propan-2-ylpyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid

Molecularweight : 481.539 g/mol

Description : White Colored powder

Melting point : 155ºC - 160ºC

Solubility : Sparingly soluble in Water

EXPERIMENTAL WORK

Preformulation Studies

Identification tests for Rosuvastatin

A) Organoleptic properties of Rosuvastatin

The Rosuvastatin was studied for color, odor and appearance.

Melting point

The melting point of Rusuvastatin was determined in a melting point apparatus known as Thiel's tube by capillary method. Capillary was sealed from one end and sample was filled in it. [2] The sample was melted and the temperature was note down

Determination of λmax of Rosuvastain

Rosuvastatin 100mg was accurately weighed and dissolved in 100ml methanol to form stock solution 1000ug/ml, then the stock solution was further diluted suitably with methanol to get working standard solution of 100ug/ml further diluted to give 10ug/ml Scaned in uv range to get λmax.

Calibration curve of Rosuvastatin

Rosuvastatin 100mg was accurately weighed and dissolved in 100ml methanol to form stock solution 1000ug/ml,then the stock solution was further diluted suitably with methanol to get working standard solution of 100ug/ml further diluted to give 2,4,6,8,10ug/ml respectively, the calibration curve was plotted by considering absorbance on Y-axis and concentration on X-axis. [3]

Preparation of Reagent

PH 6.8 Phosphate Buffer Solution

Dissolve 28.80g of disodium hydrogen phosphate and 11.45 g potassium dihydrogen phosphate in sufficient water to produce 1000 ml.

Solubility study of Rosuvastatin in different solvents.

A) Dichloromethane

Add sufficient quantity of Rosuvastatin so that form a clear solution in 5ml of dichloromethane sonicate for 15 min then stirred continuously on magnetic stirrer for 48 hours after that pippte 1ml solution diluted to give 10ml then further two more dilutions give 10ml solution, determine the absorbance on uv at 244 λmax. [4]

B) Methanol

Add sufficient quantity of Rosuvastatin so that form a clear solution in 5ml of methanol sonicate for 15 min then stirred continuously on magnetic stirrer for 48 hours after that pippte 1ml solution diluted to give 10ml then further two more dilutions give 10ml solution, determine the absorbance on uv at 244 λmax. [5]

C) Ethanol

Add sufficient quantity of Rosuvastatin so that form a clear solution in 5ml of ethanol sonicate for 15 min then stirred continuously on magnetic stirrer for 48 hours after that pippte 1ml solution diluted to give 10ml then further two more dilutions give 10ml solution, determine the absorbance on uv at 244 λmax. [6]

D) Water

Add sufficient quantity of Rosuvastatin so that form a clear solution in 5ml of Water sonicate for 15 min then stirred continuously on magnetic stirrer for 48 hours after that pippte 1ml solution diluted to give 10ml then further two more dilutions give 10ml solution, determine the absorbance on uv at 244 λmax. [7]

Phosphate buffer 6.8

Add sufficient quantity of Rosuvastatin so that form a clear solution in 5ml of Phosphate buffer 7.4 sonicate for 15 min then stirred continuously on magnetic stirrer for 48 hours after that pippte 1ml solution diluted to give 10ml then further two more dilutions give 10ml solution, determine the absorbance on uv at 244 λmax.

Formulation of solid Dispersion

Rosuvastatin solid dispersions by solvent evaporation method

Solid dispersion of RSV with Poly Vinyl Alcohol and Poly Acrylic Acid in different weight ratios were prepared by the solvent evaporation method. Accurately weighed amount of drug and carriers in various ratios dissolved in Dichloromethane in a round bottom flask and the solvent was evaporated at 45°C temperature. Solid dispersions were subsequently stored in a vacuum

oven at room temperature for 48 h to remove the residual solvent. [8] The dried solid dispersions were grinded in a mortar and pestle and passed through sieve no. 60 and were stored in desiccators until use.

Formulation of Rosuvastatin Tablet.no 1.

Sr. No	Composition (mg)	Formulation Code				
		F1	F2	F3	F4	F5
01	Rosuvastatin SD Equal to (10 mg)	SD A1	SD A2	SD A3	SD A4	SD A5
02	Rosuvastatin SD Equal to (10 mg)	SD B1	SD B2	SD B3	SD B4	SD B5
03	DCP	30	30	30	30	30
04	MCC	66.5	66.5	66.5	66.5	66.5
05	Talc	5	5	5	5	5
06	Magnesium stearate	5	5	5	5	5
Total Weight = (mg)		150	150	150	150	150

RESULTS AND DISCUSSION

Preformulation Studies

Identification tests for Rosuvastatin

A) Organoleptic properties of Rosuvastatin Organoleptic characters of drug was observed and recorded by using descriptive terminology. The following properties of drug were studied.

Table No.2:Organoleptic Properties of Rosuvastatin

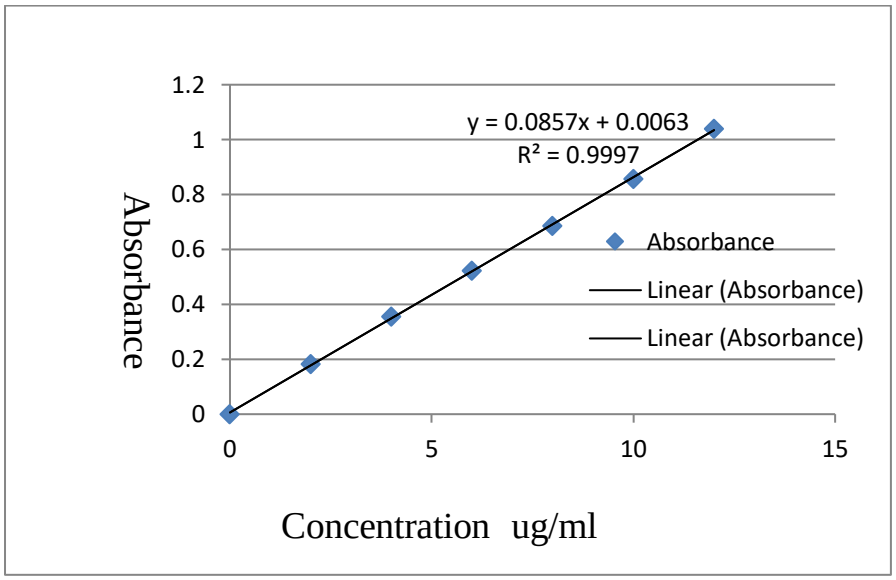
Sr. No.	Property	Result
1.	Colour	White Powder
2.	Odour	Odourless
3.	Teste	Bitter

B) Melting point of Rosuvastatin

The melting point of Rosuvastatin determined by capillary method was found to be 216^0C -218^0C.

C) Calibration curve of Rosuvastatin

A solution of 100 µg /ml of Rosuvastatin was scanned in the range of 400 to 200 nm. The drug exhibited the λ max at 244 nm and showed reproducibility.[9] The standard curve of Rosuvastatin in methanol was obtained that obeys the Beers-Lambert's law in the range 2-20 µg/ml in the medium as shown in TableNo.9.



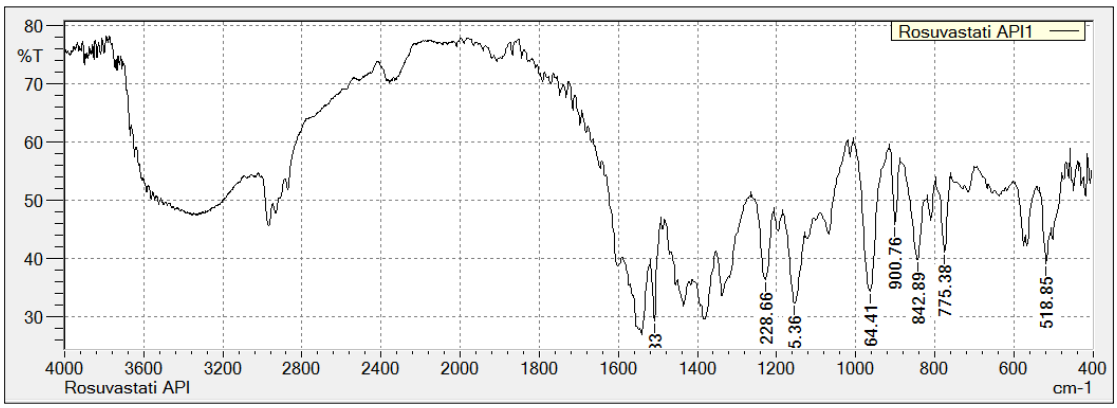


FIG: 1 FTIR Spectra of Rosuvastatin

In vitro dissolution studies

Preformulation Study

1) **Characterization of Rosuvastatin Optimized Batch Solid Dispersion by using Polyvinyl Alcohol & Poly Acrylic Acid**

Table no :3

SD Ratio	% yield of SD	Angle of repose(⌧)	Bulk Density	Tapped Density	Carr, s Index	Hauseners Ratio	Drug content
1:2	98.5	25.45	0.3806	0.3430	90.12	0.9021	97.34%

B) Weight Variation

Table no :4

Tablet Weight	Weight variation
154	2.4
150	-0.19
150	-0.19
149	-0.86
150	-0.19
151	0.46
150	-0.19
152	1.1
150	-0.19
149	-0.86
148	-1.5
148	-1.5
150	-0.19
150	-0.19
151	0.46
150	-0.19
152	1.1
151	0.46
150	-0.19
Average Weight	150.35

2) Disintegration Test

Table no :5

Tablet Number	Disintegration time
1	10
2	12
3	10
4	13
5	12

3) Drug Content

Table no:5

Tablet Number	Rosuvastatin % Content
1	90.2& 93.5 %
2	86.5 & 67.9 %
3	90.1& 85.5 %
4	92.5 & 86.5 %
5	94.2 & 90.56 %

SUMMARY AND CONCLUSION

Statins are effective medicine. Statins can effectively stabilise or reverse plaque, improve prognosis, and reduce mortality and morbidity by lowering blood lipid levels and inhibiting the inflammatory response within the already present atherosclerotic plaque.

In this context, this research aims to investigate the preparation of Fixed dose combination solid dispersions composed of antihyperlipidemic agents , will prepare by solvent evaporation techniques, Formulation and process parameters will test and the obtain formulations will evaluate with the physicochemical and functional characterization. The aim of the present study was to improve solubility and drug release of two FDCs each containing two poorly soluble drugs with opposite ionisation properties. The two compounds in each FDC showed opposing pH-dependent solubility in media simulating pH conditions of different sites of the GI tract, that is, the weak acids are better soluble at the higher pH values present in the small intestine, while the reverse is true for the weak bases which have higher solubility in the stomach.

REFERENCES

1. Aftab Modi , Pralhad Tayade, "Enhancement of dissolution profile by solid dispersion (kneading) technique AAPS Pharm SciTech", Aug 2006. Anshu S, Jain CP, Preparation and characterization of solid dispersions of valsartan with poloxamer. Scholars Research Library 188. Der Pharm Lett, 2(2):54-63 2010.

2. Bhaskar D, Chella N, Sateesh KV and Rama RT. "Solubility and dissolution enhancement of flurbiprofen by solid dispersion using hydrophilic carriers". Brazilian Journal of Pharmaceutical Sciences, 2017;53(4):e00010 Fule R, Amin P. development and evaluation of lafutidine solid dispersion via hot melt extrusion: Investigating drug-polymer miscibility with advanced characterization, Asian journal of pharmaceutical sciences,2 0 1 4;1-15.

3. Khalid Bashir Mir, Nisar Ahmed Khan, "solid dispersion: overview of the technology IJPSR", 2017; Vol. 8(6): 2378-2387. Linda F. Remington, Essentials of Pharmaceutics. 1st ed. USA: Pharmaceutical Press, 2006;p. 238. Maraie NK, alhamdany AT, Radhi AA. efficacy of combination solid dispersion technology on dissolution performance of nalidixic acid and Cefdinir asian journal of pharmaceutics and clinical research, vol 10, issue 4. Mounica 2017.

4. V, Shekhar SR, Vijayalakshmi P. "Formulation and evaluation of rosuvastatin solid dispersions" World journal of pharmaceutical sciences, 2015; 2321-3086. INSTITUTE OF PHARMACEUTICAL SCIENCE AND RESEARCH (IPSR), BALAGHAT Page9 Phuong Tran , Yong-Chul Pyo , Overview of the Manufacturing Methods of Solid Dispersion Technology for Improving the Solubility of Poorly Water-Soluble Drugs and Application to Anticancer Drugs MDPI,19 March 2019.

5. Rakesh Tiwle "An Exhaustive Review On Solubility Enhancement For Hydrophobic Compounds By Possible Applications Of Novel Techniques." Science Alert –Trends Research In Applied Science And Research. 7(8): 596-619; 2012

6. Rashmi V. Trivedi, Pravin S. Admane, Jayashree B. Taksande, Jayashri G. Mahore and Milind J. Umekar. “Solubility enhancement studies of hydrochlorothiazide by preparing solid dispersions using losartan potassium and urea by different methods”, Scholars Research Library Der Pharmacia Lettre, 3 (6):8-17 2011

7. Riekesa MK, Dereymakera A, Berbena P, Augustijnsa P, Stulzerb HK, Mootera GV. “Development of enteric-coated fixed dose combinations of amorphous solid dispersions of ezetimibe and lovastatin”: Investigation of formulation and process parameters, International journal of Pharmaceutics, 520, 49–58. 2017

8. Save T, Venkitachalam P. “studies on solid dispersions of nifedipine drug development and industrial pharmacy”, 18(15), 1663-1679. 1992

9. Siahi-Shadbad MR, Ghanbarzadeh S, Barzegar-Jalali M, Valizadeh H, Taherpoor “A, Mohammadi G. Development and characterization of solid dispersion for dissolution improvement of furosemide by cogrinding method”. Advanced Pharmaceutical Bulletin, 4(4):391-9. 2014