JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

SOLUBILITY ENHANCEMENT OF ROSUVASTATIN CALCIUM USING SOLVENT EVAPORATION TECHNIQUE

Dr. Drashti A. Mandale, Matadar Mo. Nauman, Mistry Janvi, Modi Isha, Modi Nandini, Motli Hasan, Dr. Nidhi N. Chauhan

Abstract

Preparation of Rosuvastatin Calcium by Using HPMC Polymers and Solid Dispersion Method, Rosuvastatin calcium is a Dyslipidemic agent, which act as a selective competitive inhibitor of HMG CoA educates enzyme and is used in the treatment of hyperlipidemia. In the present work, Solid Dispersion was prepared by solvent evaporation method to increase the solubility of Rosuvastatin Calcium. Solid dispersions were evaluated by determining percentage yield, in vitro dissolution profile. The prepared solid dispersion is formulated into Tablet dosage form and characterized by various parameters i.e., weight variation, Friability, Hardness, and dissolution. The evaluated parameters of Tablet dosage form increase in solubility and dissolution rate of the pure drug.

Key words: Solvent evaporation technique, Rosuvastatin, Bioavailability, Polymer-HPMC.

1. INTRODUCTION

1.1 Solubility [1]

Solubility is defined as the maximum amount of solute dissolve in the given amount of solvent or the concentration of solute in saturated solution at a certain temperature, pressure, or presence of certain chemical. The solubility of a substance depends on the solvent used as well as on temperature and pressure. The extent of solubility of a substance in a specific solvent is measured as the saturation concentration where adding more solute does not increase its concentration in the solution.

Solute: It is a substance which is present in small quantity and dissolves in the solvent.

Solvent: It is the component which forms the main constituent of a solution and it is also capable of dissolving another substance to form a consistently disperse mixture at a molecular level.

1.1.1 Solubility Expression

Table 1.1.1: Solubility Expression

Conditions	Parts Solvent required for Parts of Solute
Very soluble	≤1
Freely soluble	1 to 10
Soluble	10 to 30
Sparingly soluble	30 to 100
Slightly soluble	100 to 1000
Very slightly soluble	1000 to 10,000
Practically soluble or insoluble	10,000 or more

IUPAC defines solubility as the analytical composition of a saturated solution expressed as a proportion of a designated solute in a designated solvent. Solubility may be stated in units of concentration, molality, mole fraction, mole ratio, and other units.

1.1.2 Process of Solubilization [2]

Step 1: The process of solubilization involves the breaking of interionic or intermolecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, interaction between the solvent and the solute molecule or ion.

Step 2: Molecule of the solid breaks away from the bulk.

Step 3: The feed of solid molecule is integrated into the hole in Solvent.

The drugs can be classified in to four basic groups on the bases of their solubility and permeability GIT mucosa. This system of classification is called as Biopharmaceutical classification system (BCS)

Biopharmaceutics classification system (BCS) was introduced by US Food and Drug Administration (FDA) and it classify the drug in to four classes according to permeability and solubility. Solubility impediment are faced in the Class II and Class IV of the system facing dissolution as the rate limiting step for the absorption of drug due to low solubility.

1.1.3 BCS classification of Drug [2]

Table 1.1.3: BCS Classification of Drug

Class	Permeability	Solubility
I	High	High
II	High	Low
III	Low	High
IV	High	High

Class I: Drugs belonging to this class have high solubility & High permeability. e.g., Metoprolol, Diltiazem, Verapamil, Propranolol.

Class II Drugs belonging to this class have low solubility & high permeability e.g., Phenytoin, Danazol, Ketoconazole, Mefenamic acid, Nifedipine.

Class III Drugs belonging to this class have high solubility & low permeability. e.g., Cimetidine, Acyclovir, Neomycin B, Captopril.

Class IV Drugs belonging to this class have low solubility & low permeability. Taxol, Griseofulvin.

1.1.4 Factors Affecting Solubility [2]

2 **Particle size**: Particle size affects solubility. As article size decreases, the surface area to volume ratio increases. As the surface area of particle increases it causes greater interaction with solvent. The effect of particle size on solubility can be described by,

3 **Temperature**: Solubility affected by temperature. If the solution process absorbs energy, then the solubility will increase with increasing temperature. If the solution process releases energy, then the solubility will decrease with increasing temperature.

4 **Molecular size:** The solubility of the substance is decreased when molecules have higher molecular weight and higher molecular size because larger molecules are more difficult to surround with solvent molecules in order to solvate the substance.

5 **Nature of solute and solvent:** The nature of solute and solvent depends on concentration of solute in specific quantity of solvent at specific temperature. Example: at room temperature in 100gm of water only 1gm of lead (II) chloride can be dissolved while 200 grams of zinc chloride can be dissolved.

6 **Pressure:** For gaseous solutes, an increase in pressure increases solubility and a decrease in pressure decrease the solubility. For solids and liquid solutes, changes in pressure have no effect on solubility.

7 **Polarity:** Polarity of both solute and solvent molecules affects the solubility. Generally polar solute molecules will dissolve in polar solvents and non-polar solute molecules will dissolve in non-polar solvents.

8 **Polymorphs:** The ability of a substance to crystallize in more than one crystalline form is polymorphism. Polymorph is an agent having ability to crystallize in more than one crystalline form. It is possible that solid can crystallize in different forms or polymorphs. Polymorphs can vary in melting point. Since the melting point of the solid is related to solubility, so polymorphs will have different solubility.

1.1.5 TECHNIQUES TO OVERCOME POOR SOLUBILITY [2,6]

I. Chemical Modifications:

1) Salt Formation
2) Co-crystallization
3) Co-solvency
4) Hydrotropy
5) Use of novel solubilizer
6) Nanotechnology

II. Physical Modifications:

1. Particle size reduction

a) Conventional method
b) Micronization
c) Nanosuspension

2. Modification of the crystal habit

a) Polymorphs
b) Pseudopolymorphs

3. Complexation

a) Physical mixture

b) Kneading method

c) Co-precipitate method

4. Inclusion Complex Formulation Based Techniques

a) Kneading method

b) Lyophilization/ Freeze- drying Technique

c) Microwave irradiation method

5. Solubilization by surfactants

a) Microemulsions

b) Self microemulsifying drug delivery system

6. Drug dispersion in carriers

a) Solid solutions

b) Solid dispersions

i. Fusion Process
ii. Solvent Method
iii. Fusion solvent method
iv. Spray drying
v. Lyophilization (Spray Freeze Drying Method)
vi. Hot melt Extrusions
vii. Dropping Method.

1.2 Dyslipidemia [3]

Dyslipidemia is elevation of plasma cholesterol, triglycerides of both, or a low high- density lipoprotein cholesterol level that contributes to the development of atherosclerosis Cause may be primary or secondary. Diagnosis is by measuring plasma levels of total cholesterol, 1Ow and individual lipoproteins. Treatment involves dietary changes, exercise, and lipid- lowering drugs.

1.2.1 Drug Therapy [4]

1) HMG -CoA reductase inhibitors (statin

2) Fibrates

3) Bile acid binding resins

4) Omega 3 fatty acid

1.2.2 Classification of HMG CoA Reductase inhibiters [4]

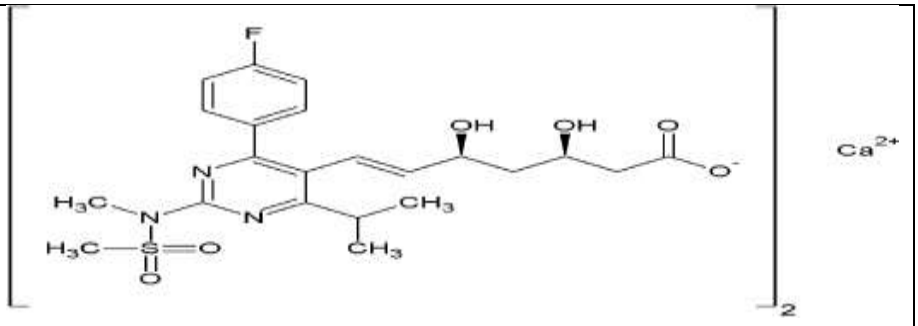
- Atorvastatin
- Rosuvastatin calcium
- Lovastatin
- Fluvastatin
- Pitavastatin
- Pravastatin
- Simvastatin

1.2.3 Mechanism of Action of rosuvastatin calcium [4]

Statin competitively inhibit HMG-CoA reductase, the rate-limiting step in cholesterol biosynthesis (i.e., the conversion of HMG-CoA to mevalonate). This results in a decrease in blood LDL and VLDL levels. Decrease Cholesterol synthesis increase LDL receptors in the liver, increase LDL uptake and degradation. Thus, statins are very effective in reducing plasma LDL levels. They also reduce triglycerides (TGs) and increase HDL-cholesterol levels in plasma. Statins (those with short half-life) are usually given once daily in the evening because cholesterol biosynthesis occurs mainly at night. Atorvastatin and rosuvastatin have long half-life.

Drug profile of Rosuvastatin Calcium [5,7]

SR NO.	PARAMETER	ROSUVASTATIN CALCIUM
1.	CATEGORY	Antihyperlipidemic, HMG-CoA Reductase Inhibitor

2.	STRUCTURE	
3.	CHEMICAL FORMULA	$C_{44}H_{54}CaF_2N_6O_{12}S_2$
4.	IUPAC NAME	Calcium bis(3R,5S,6E)-7-[4-(4-flurophenyl)-2-(N-methylmethanesulfonamido)-6-(propan-2-yl) pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate)
5.	CAS NUMBER	147098-20-2
6.	MOLECULAR WEIGHT	1001.1 gm/mol
7.	CHARACTERISTIC	An off-white to creamish white crystalline powder
8.	Pka	Pka (Acidic) 4 Pka (Basic) 2.8
9.	SOLUBLITY	Sparingly soluble in water and methanol, and slightly soluble in ethanol
10.	PHARMACOLOGY OF ROSUVASTATIN CALCIUM	Rosuvastatin calcium is in a class of medication called HMG-CoA reductase inhibitors (statins). It works by slowing the production of cholesterol in the body to decrease the amount of cholesterol that may build up on the walls of the arteries and block blood flow to the heart, brain, and other parts of the body.

2. Materials and Methods

2.1 Melting point

Procedure:

- Place a capillary tube, sealed at one end with the open end facing down, into 0.5 cm^3 of rosuvastatin calcium in to micro test tube. Attach the micro test tube to a thermometer with a thread.
- Clamp the micro test tube and thermometer in the minimal glycerin, making sure neither test tube nor thermometer is in contact with the glass walls of the Thiele tube.
- Move a small Bunsen flame back and forth the lower part of the side arm of the Thiele tube. An initial stream of bubbles will come from the open end of the capillary tube.
- Continue heating until rapid and continuous steam of bubbles comes from the capillary tube. Stop heating and record the temperature as soon as rosuvastatin calcium is drawn up into the capillary tube.

2.2 Calibration curve of rosuvastatin calcium

2.2.1 Preparation of calibration curve in phosphate buffer (pH 6.8)

10 mg of rosuvastatin calcium were dissolved in a tiny quantity of methanol (used as a co-solvent) and diluted in 100 ml of phosphate buffer. pH6.8. A stock solution of 250g/ml was prepared by diluting 50 ml of this solution to 100 ml with phosphate buffer pH6.8 to make a stock solution. Take 0.1, 0.2, 0.3, 0.4, 0.6 and 0.8 ml of this stock solution and transfer it to a 10 ml volumetric flask with phosphate buffer to make it up to 10 ml. Using phosphate buffer as a blank, the absorbance of these solutions was measured at 241 nm.

2.2.2 Preparation of calibration curve in methanol

10 mg of Rosuvastatin Calcium was dissolved in 100 ml methanol and 50 ml of this solution was taken and diluted to 100 ml again with methanol to prepare a stock solution of 250µg/ml as a stock solution. From this stock solution, aliquots of 0.1, 0.2, 0.3, 0.4, 0.6 and 0.8 and transferred to 10 ml volumetric flask and volume was made up to 10 ml with methanol. The absorbance of these solutions was measured at 238 nm using methanol as blank.

2.2.3 Preparation of calibration curve in water

10 mg of Rosuvastatin Calcium was dissolved in 100 ml water and 50 ml of this solution was taken and diluted to 100 ml again with water to prepare a stock solution of 250µg/ml as a stock solution. From this stock solution, aliquots of 0.1, 0.2, 0.3, 0.4, 0.6 and 0.8 and transferred to 10 ml volumetric flask and volume was made up to 10 ml with water.

3. Solvent evaporation

3.1. In this method, the first step is formation of solution containing physical mixture of the drug and carrier dissolved in a common solvent (Acetone and Methanol) and second step involve the removal of solvent resulting the formation of solid dispersion. This enabled them to produce a solid solution of the highly lipophilic drug in a highly water-soluble carrier HPMC. An important prerequisite for the manufacture of a solid dispersion using the solvent evaporation method is that both the drug and the carrier are sufficiently soluble in the solvent. The solvent can be removed by trituration method with the help of mortar and pestle.

Rosuvastatin calcium and several water-soluble carries (HPMC) were weighed in varied ratios of 1:1, 1:3, 1:5. The tablets were punched for each drug polymer (1:1, 1:3, 1:5) and for pure API also.

3.2. Pre compression study

3.2.1. Angle of Repose

The funnel technique was used to calculate angle of repose.

Equation is used to determine the angle of repose: $\tan\theta = h/r$

Where h = height of pile

r = radius of the base of the pile

θ = angle of repose

3.2.2. Bulk Density

Weighed quantity of the powder (W) is taken in a graduated measuring cylinder and volume (V0) is measured and bulk density is calculated using the formula

(BD) = W/c

W =Weight of the powder,

$\mathbf{V_0}$ =Volume of powder

3.2.3.Tapped Density

(TD) = W/Vf

W=Weight of the powder

V f =Volume of powder

3.2.4 Carr's Index

$$\text{Carr's index} = \frac{\text{Tapped density}}{\text{Bluck density}} \text{ X } 100$$

3.2.5. Hausner's Ratio

$$\text{Hausner's Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

3.2.6. %Yield

$$\%\text{Yield} = \frac{\text{Practical Yield}}{\text{Theoritical Yield}}$$

4. Pre compression tests:

4.2.1. Hardness testing

The hardness of tablets was determined using a Monsanto meter hardness tester.

4.2.2. Weight variation test

20 tablets were selected at random, weighed, and the average weight was calculated. No more than of the individual weights should deviate from the average weight by more than 7.5%.

4.2.3. Friability test

For each formulation, a pre-weighted tablet sample (5 tablets) was placed in a friability, which is then operated for 100 revolutions. Then tablets were reweighted. compressed tablets that lose not more than 1% of their weight are considered acceptable.

4.2.4. In vitro dissolution study

In vitro drug release study of prepared batches (n=3) was performed using USP (United States Pharmacopoeia) apparatus II fitted with a paddle (75 rpm). The percentage drug release was calculated up to 30 min (Sampling time 5,10,15,20,25,30 min) in Phosphate buffer was added to the dissolution basket. At predetermined time intervals, 5 ml samples were withdrawn.

5. RESULT AND RECORD:

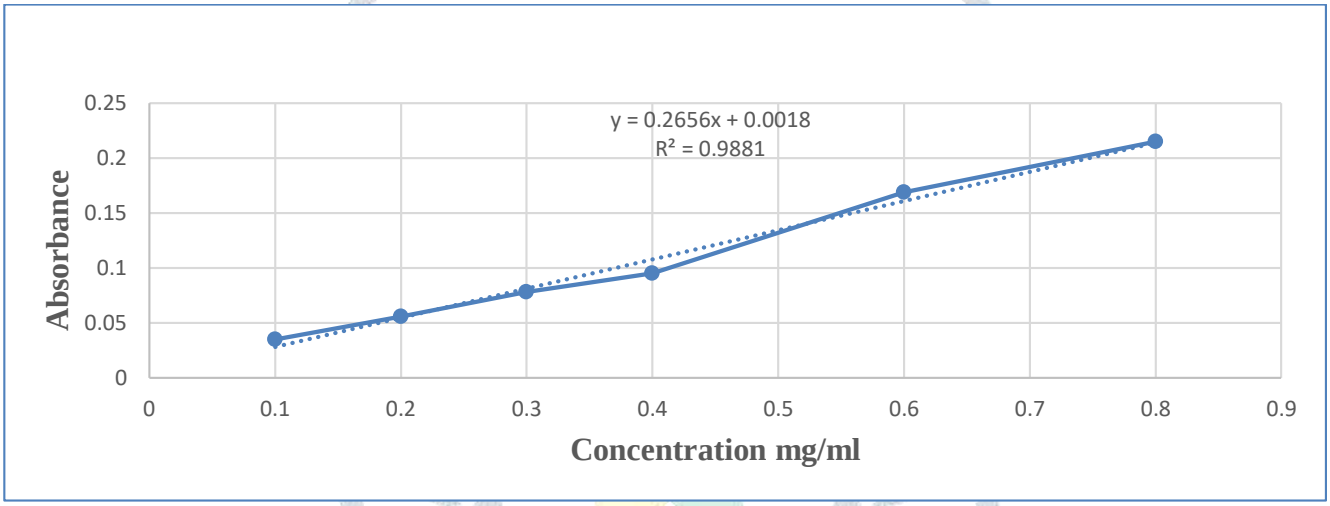
5.1. Melting point

Table 5.1. Melting point

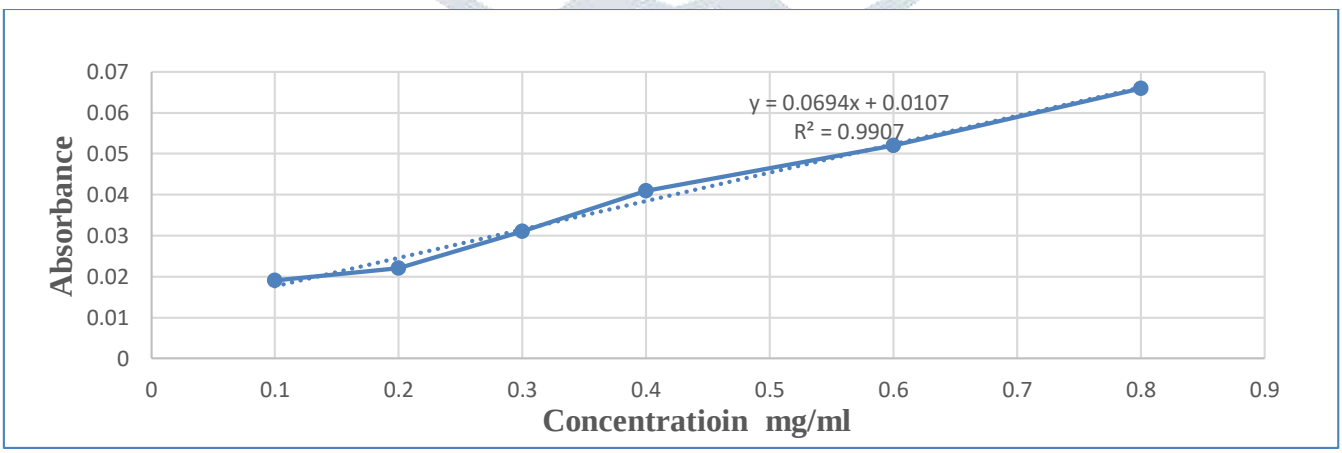
Sr no.	Reported melting point	Observed melting point
1	173-185^{0}C	170-172^{0}C

5.2. Calibration Curve of Rosuvastatin Calcium in Different Solvent

5.2.1. Calibration curve of rosuvastatin calcium in phosphate buffer solution



5.2.2. Calibration curve of rosuvastatin calcium in methanol



5.2.3 Calibration curve of rosuvastatin calcium in water

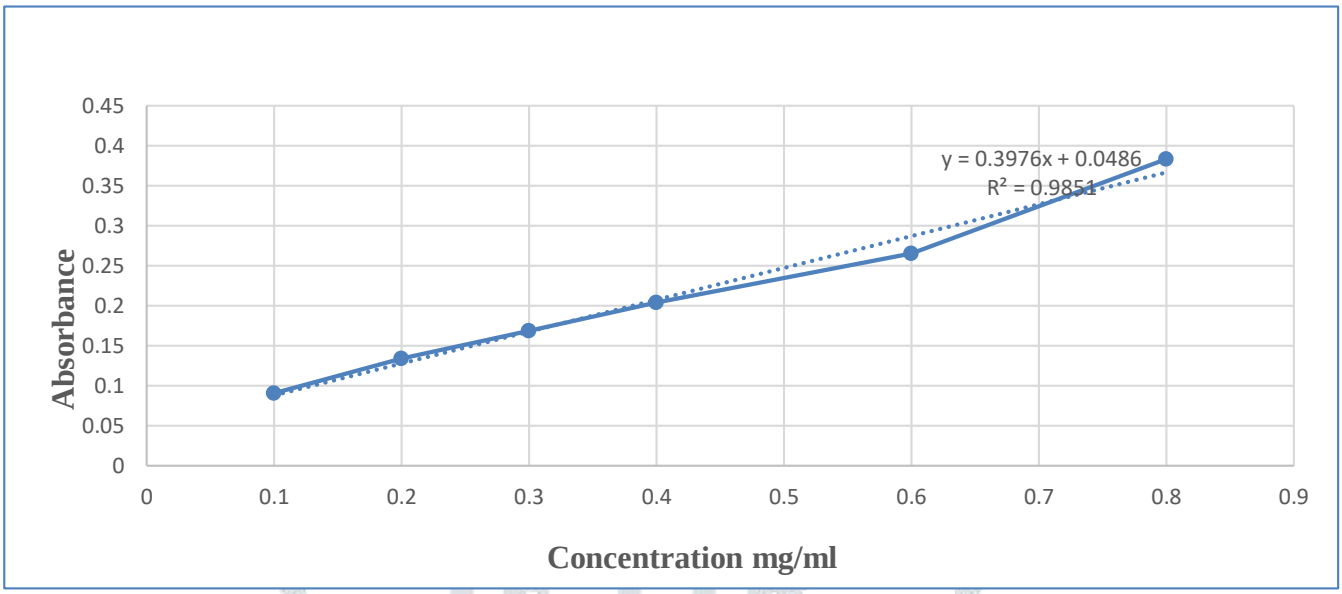


Table 5.3 Result for Solubility of SD Obtain using Solvent Evaporation

Sr no.	Solvent	Polymer	Ratio Drug to Polymer (HPMC)	Drug (In gm)	Polymer (In gm)	Saturation Solubility	
						mg/ml	fold
1.	Methanol	-	1:0	1	-	0.400	1
		HPMC	1:1	1	1	1.29	3.22
			1:3	1	3	2.09	5.22
			1:5	1	5	2.99	7.475
2.	Acetone	-	1:0	1	-	0.597	1
		HPMC	1:1	1	1	1.45	2.42
			1:3	1	3	2.15	3.60
			1:5	1	5	3.05	5.10

6. Post compression test

Table 6.1. % Yield of solid dispersion using solvent Evaporation

Sr no	Solid dispersion	Polymer	Ratio	Drug (in gm)	Polymer (in gm)	Theoretical weight	Weight of solid dispersion	Yield (%)
1	Solvent Evaporation	HPMC	1:1	1	1	2	1.78	88%
2			1:3	1	3	4	3.65	91.25 %
3			1:5	1	5	6	5.86	97.67 %
4	Solvent Evaporation	HPMC	1:1	1	1	2	1.89	94.5%
5			1:3	1	3	4	3.92	98%
6			1:5	1	5	6	5.96	99.3%

Table 6.2. Pre-Compression Test of Rosuvastatin Calcium

Drug polymer ratio in acetone	Angle of repose	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index	Hausner's ratio
1:1	30.10	0.444	0.543	18.23	1.223
1:3	32.72	0.439	0.549	20.03	1.249
1:5	30.74	0.464	0.529	16.88	1.140
Drug polymer ratio in methanol	**Angle of repose**	**Bulk density (g/ml)**	**Tapped density (g/ml)**	**Carr's index**	**Hausner's ratio**
1:1	29.48	0.453	0.571	13.135	1.152
1:3	33.25	0.468	0.519	13.331	1.153
1:5	30.98	0.481	0.555	14.884	1.202

6.3. Post compression test

6.3.1. Hardness test

Table 6.3.1.1 Hardness test of drug and polymer mixture

Sr no.	Drug polymer ratio in Acetone	Tab 1 (kg/cm^2)	Tab 2 (kg/cm^2)	Tab 3 (kg/cm^2)	Average (kg/cm^2)
1.	1:1	4	4.5	4	4.16
2.	1:3	4.5	4.5	5	4.67
3.	1:5	6	6	6.5	6.16

Table 6.3.1.2 Hardness test of drug and polymer mixture

Sr no.	Drug polymer ratio in Methanol	Tab 1 (kg/cm^2)	Tab 2 (kg/cm^2)	Tab 3 (kg/cm^2)	Average (kg/cm^2)
1.	1:1	3.5	3	3.5	3.33
2.	1:3	4	5	4	4.33
3.	1:5	6.6	6	6.5	6.36

Table 6.3.1.3 Hardness test of pure and marketed tablets

Sr no.	Hardness of pure tablets (kg/cm^2)
1.	9
2.	8
3.	8
Average	**8.34**

Sr no.	Hardness of marketed tablets (kg/cm^2)
1.	10
2.	10.5
3.	10.5
Average	**10.34**

6.3.2 Weight Variation Test:

Table 6.3.2.1: Drug Polymer Mixture

Sr No.	1:1 Methanol (In gm)	1:3 Methanol (In gm)	1:5 Methanol (In gm)
1	0.248	0.246	0.241
2	0.245	0.244	0.246
3	0.253	0.254	0.253
4	0.254	0.251	0.251
5	0.243	0.251	0.255
6	0.251	0.249	0.247
7	0.250	0.245	0.248

8	0.249	0.249	0.243
9	0.254	0.253	0.249
10	0.243	0.250	0.251
11	0.247	0.253	0.255
12	0.251	0.248	0.247
13	0.248	0.246	0.252
14	0.248	0.252	0.253
15	0.252	0.256	0.250
16	0.253	0.255	0.246
17	0.251	0.249	0.249
18	0.246	0.248	0.248
19	0.247	0.251	0.254
20	0.245	0.254	0.251
Average Weight	**0.236**	**0.250**	**0.249**

- **All Tablets pass weight variation test.**

Table 6.3.2.2: Drug Polymer Mixture

Sr No.	1:1 Acetone (In gm)	1:3 Acetone (In gm)	1:5 Acetone (In gm)
1	0.251	0.249	0.255
2	0.246	0.246	0.252
3	0.243	0.252	0.246
4	0.253	0.248	0.249
5	0.241	0.254	0.254
6	0.251	0.243	0.253
7	0.249	0.253	0.250
8	0.243	0.255	0.244
9	0.248	0.251	0.249
10	0.252	0.248	0.256
11	0.254	0.246	0.243
12	0.247	0.256	0.253
13	0.252	0.252	0.256
14	0.246	0.247	0.249
15	0.251	0.249	0.250
16	0.250	0.244	0.248
17	0.246	0.254	0.245
18	0.249	0.251	0.253
19	0.253	0.250	0.254
20	0.252	0.248	0.249
Average Weight	**0.248**	**0.237**	**0.262**

- **All Tablets pass weight variation test.**

Table 6.3.2.3: Weight Variation for Pure Drug Tablet

Sr no.	Weight of Pure Tablet (In gm)	Sr no.	Weight Variation of Tablet (in gm)
1	0.245	11	0.235
2	0.247	12	0.240
3	0.238	13	0.244
4	0.244	14	0.247
5	0.236	15	0.241
6	0.243	16	0.237
7	0.242	17	0.239
8	0.249	18	0.243
9	0.248	19	0.247
10	0.238	20	0.249
Average Weight		**0.242**	

- **All Tablets pass weight variation test.**

Table 6.3.2.4 Weight Variation of Marketed Tablet:

Sr no.	Weight of Marketed Tablets (In gm)	Sr no.	Weight of Marketed Tablets (In gm)
1	0.133	11	0.134
2	0.134	12	0.136

3	0.132	13	0.130
4	0.132	14	0.129
5	0.130	15	0.139
6	0.135	16	0.137
7	0.136	17	0.138
8	0.133	18	0.131
9	0.131	19	0.135
10	0.130	20	0.133
Average Weight		**0.133**	

All Tablets pass weight variation test.

6.3.3. Friability test

Table 6.3.3.1: Drug polymer ratio in acetone (1:1)

Sr no.	Initial Weight	Final Weight	Friability (%)
1	0.213	0.212	0.46
2	0.207	0.206	0.48
3	0.215	0.214	0.46
4	0.218	0.217	0.45
5	0.215	0.214	0.46

Table 6.3.3.2 Drug polymer ratio in acetone (1:3)

Sr no.	Initial Weight	Final Weight	Friability (%)
1	0.235	0.233	0.85
2	0.227	0.226	0.44
3	0.236	0.234	0.84
4	0.229	0.227	0.87
5	0.230	0.228	0.86

Table 6.3.3.3 Drug polymer ratio in acetone (1:5)

Sr no.	Initial weight	Final weight	Friability (%)
1	0.240	0.238	0.83
2	0.245	0.244	0.40
3	0.249	0.247	0.80
4	0.239	0.237	0.83
5	0.242	0.240	0.82

Table 6.3.3.4 Drug polymer ratio in methanol (1:1)

Sr no.	Initial weight	Final weight	Friability (%)
1	0.220	0.218	0.90
2	0.209	0.207	0.94
3	0.216	0.215	0.46
4	0.216	0.215	0.48
5	0.211	0.210	0.47

Table 6.3.3.5 Drug polymer ratio in methanol (1:3)

Sr no.	Initial weight	Final weight	Friability (%)
1	0.224	0.223	0.44
2	0.222	0.221	0.45
3	0.220	0.219	0.47
4	0.226	0.224	0.88
5	0.228	0.227	0.43

Table 6.3.3.6 Drug polymer ratio in methanol (1:5)

Sr no.	Initial weight	Final weight	Friability (%)
1	0.234	0.233	0.42
2	0.237	0.235	0.84
3	0.236	0.234	0.84
4	0.230	0.229	0.43
5	0.231	0.230	0.43

Table 6.3.3.7 Friability test for pure drug

Sr No.	Initial Weight	Final Weight	Friability (%)
1	0.245	0.243	0.80
2	0.247	0.245	0.80
3	0.238	0.237	0.42
4	0.244	0.243	0.40
5	0.236	0.235	0.42

Table 6.3.3.8 Friability test for marketed tablets

Sr no.	Initial weight	Final weight	Friability (%)
1	0.133	0.132	0.75
2	0.134	0.133	0.74
3	0.132	0.131	0.75
4	0.132	0.131	0.75
5	0.130	0.129	0.74

6.3.4. In vitro dissolution test

Table 6.3.4.1 In vitro dissolution test for Drug polymer ratio in acetone (1:1)

Sr no.	Drug polymer ratio in acetone	Time	Absorbance	% drug release
1.	1:1	5	0.485	55.8
2.	1:1	10	0.51	57.82
3.	1:1	15	0.556	62.45
4.	1:1	20	0.625	73.5
5.	1:1	25	0.696	83.88
6.	1:1	30	0.71	94.89

Table 6.3.4.2 In vitro dissolution test for Drug polymer ratio in acetone (1:3)

Sr no.	Drug polymer ratio in acetone	Time	Absorbance	% drug release
1	1:3	5	0.477	62.5
2	1:3	10	0.537	65.10
3	1:3	15	0.631	73.32
4	1:3	20	0.665	79.98
5	1:3	25	0.729	87.23
6	1:3	30	0.738	97.77

Table 6.3.4.3 In vitro dissolution test for Drug polymer ratio in acetone (1:5)

Sr no.	Drug polymer ratio in acetone	Time	Absorbance	% drug release
1	1:5	5	0.481	75.6
2	1:5	10	0.497	79.54
3	1:5	15	0.521	81.1
4	1:5	20	0.629	84.32
5	1:5	25	0.701	91.65
6	1:5	30	0.796	99.56

Table 6.3.4.4 In vitro dissolution test for Drug polymer ratio in methanol (1:1)

Sr no.	Drug polymer ratio in methanol	Time	Abs.	%drug release
1.	1:1	5	0.435	32.44
2.	1:1	10	0.495	52.3
3.	1:1	15	0.512	62.95
4.	1:1	20	0.576	75.76
5.	1:1	25	0.698	85.76
6.	1:1	30	0.785	93.97

Table 6.3.4.5 In vitro dissolution test for Drug polymer ratio in methanol (1:3)

Sr no.	Drug polymer ratio in methanol	Time	Abs.	%drug release
1.	1:3	5	0.512	46.3
2.	1:3	10	0.525	68.19
3.	1:3	15	0.548	74.09
4.	1:3	20	0.569	84.45
5.	1:3	25	0.574	89.30
6.	1:3	30	0.58	96.97

Table 6.3.4.6 In vitro dissolution test in Drug polymer ratio in methanol (1:5)

Sr no.	Drug polymer ratio in methanol	Time	Abs.	%drug release
1.	1:5	5	0.49	59.55
2.	1:5	10	0.533	72.68
3.	1:5	15	0.565	85.11
4.	1:5	20	0.6	87.59
5.	1:5	25	0.712	92.35
6.	1:5	30	0.789	98.30

Table 6.3.4.7 In vitro dissolution test of pure Drug

Sr No.	Time (in min)	Absorbance (in nm)	% Drug release
1	5	0.335	28.8
2	10	0.389	42.5
3	15	0.421	53.70
4	20	0.598	69.79
5	25	0.625	76.4
6	30	0.762	85.88

Table 6.3.4.8 In vitro dissolution test of marketed tablets

Sr No.	Time (in min)	Absorbance (in nm)	% Drug release
1	5	0.364	38.6
2	10	0.382	49.29
3	15	0.415	60.65
4	20	0.431	72.45
5	25	0.468	82.45
6	30	0.547	92.02

Table 6.3.4.9 In vitro dissolution test of marketed tablets

Sr No.	Time (in min)	Absorbance	% Drug release
1	5	0.289	37.6
2	10	0.311	48.6
3	15	0.403	59.65
4	20	0.404	71.45
5	25	0.451	81.73
6	30	0.453	91.65

Table 6.3.4.10 In vitro dissolution test of marketed tablets

Sr No.	Time (in min)	Absorbance	% Drug release
1	5	0.322	39.67
2	10	0.366	50.63
3	15	0.368	61.86
4	20	0.385	73.90
5	25	0.398	83.98
6	30	0.401	93.70

7. Conclusion

Sr.no	Time (in min)	%Drug Release of Pure Drug	% Drug Release of Drug + Polymer (in methanol)			% Drug Release of Drug + Polymer (in acetone)			% Drug Release of Marketed Tablet
			1:1	1:3	1:5	1:1	1:3	1:5	
1	5	28.8	32.44	46.3	59.55	55.8	62.5	75.6	38.6
2	10	42.5	52.3	68.19	72.68	57.82	65.10	79.54	49.29
3	15	53.70	62.95	74.09	85.11	62.45	73.32	81.1	60.65
4	20	69.79	75.76	84.45	87.59	73.5	79.98	84.32	72.45
5	25	76.4	85.76	89.30	92.35	83.88	87.23	91.65	82.45
6	30	85.88	93.97	96.97	98.30	94.89	97.77	99.56	92.02

- Here **solvent evaporation** method is used to increase the solubility. We have taken three ratios of Drug and polymer (HPMC) (1:1,1:3,1:5).

- **1:1** have % Drug release up to **93.97 in Methanol** and **94.89 in Acetone.**
- **1:3** have % Drug release up to **96.97 in Methanol** and **97.77 in Acetone.**
- **1:5** have % Drug release up to **98.30 in Methanol** and **99.56 in Acetone.**
- From that **1:5** have highest % drug release.

From the results highlighted we can conclude that solid dispersions have considerable effect on improving the dissolution rate and hence bioavailability of a range of hydrotropic drugs.

8. REFERENCE

1. Ajay Kumar, Rajesh Kumar, Prachi Sharma, Ajit Pal Singh, Amar Pal Singh, "Formulation Development and Solubility Enhancement of Rosuvastatin Calcium by Using different Polymers and Solid Dispersion Method" Department of pharmaceutical sciences, St. Soldier Institute of Pharmacy
2. Sneha Jagtap, Chandrakant Magdum, Dhanraj Jadge, Rajesh Jagtap "Solubility Enhancement Technique: A Review" J. Pharm. Sci. & Res. Vol. 10(9), 2018
3. Michel H Davidson, Vishnu Priya Pulipati, "Dyslipidemia." 2021 https://www.msdmanuals.com/en-in/professional/endocrine-and-metabolic-disorders/lipid-disorders/dyslipidemia
4. Tara V Shanbhag, Smita Shenoy, "PHARMACOLOGY FOR MEDICAL GRADUATION" 4th Edition, January 11,2023
5. Drug profile of Rosuvastatin calcium https://go.drugbank.com/drugs/DB01098
6. Lovepreet Kaur, Taranjit Kaur, Amar Pal Singh, Ajeet pal Singh, "formulation development and solubility enhancement of rosuvastatin calcium by using hydrophilic polymers and solid dispersion method". Published by International Journal of Current Pharmaceutical Research ISSN- 0975-7066 Vol 13, Issue 6, 2021
7. Kapse Vidya N., S. Z. Chemate and V. M. Dharashive, Formulation development and solubility enhancement of Rosuvastatin Calcium tablet prepared by complexation with β-cyclodextrin by kneading method, IJPSR (2016), Vol. 7, published 01 December, 2016