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Enhancement Of Solubility Of Poorly Water-Soluble Drug By Solid Dispersion Method Formulation And Evaluation Of Rivoroxaban Capsule Dosage Form

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ABSTRACT

Rivaroxaban is an Antiplatelet/anticoagulant Drug used in the treatment of venous thromboembolism and belongs to the Biopharmaceutical classification system class II; hence it has a low solubility. So that the aim of this study is to enhance the solubility of the drug by solid dispersion method. Solid dispersion is nothing but the combination of two component one hydrophilic matrix and second hydrophobic drug. There are various methods are used for the preparation of solid dispersion in which solvent evaporation method used in the research. The solubility of rivaroxaban was increased by dissolving the different polymers with API using suitable solvent (Dichloromethane+ methanol) in three different ratios 1:0.5, 1:1, 1:1.5 and then this preparation kept for 24 hrs in Hot air oven to get solvent evaporate. The best polymer and ratio screening was done with the help of solubility study, the solubility study is done with the different buffers like Ph 6.8 phosphate buffer, 4.5 acetate buffer, 0.1N HCL, water with the help of UV spectrophotometer. The evaluation of final dosage form is done with the help of dissolution study in media 4.5 acetate buffer+ 0.2% SLS for about 2hrsat a specific time interval 10, 15, 30, 45, 60, 90, 120 minutes. Drug polymer compatibility study was done by different analysis like FTIR, XRD, DSC and SEM.

Keywords: *Rivaroxaban, Solid Dispersion, Solvent Evaporation, anticoagulant, Polymers, BCS Class II, Solubility*

1. INTRODUCTION

Rivaroxaban is an oral antiplatelet/anticoagulant drug and it is marketed as Xarelto. It is the first available orally active direct coagulating factor Xa inhibitor. It is used for the treatment of venous thromboembolism. U.S. Food and Drug Administration (FDA) Approved Rivaroxaban used for prophylaxis of deep vein thrombosis(DVT), which may lead to pulmonary embolism. Rivaroxaban is a BCS Class II Drug hence it has a low solubility to increase the solubility of API various techniques are used.

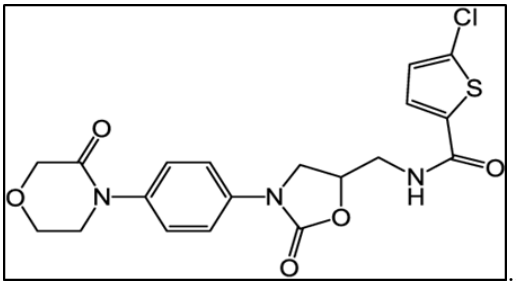


Fig 1: Structure of Rivaroxaban,

2. MATERIALS AND METHOD:

MATERIALS:

Table 1: List of Materials

Rivaroxaban	Dr. Reddy's Laboratory
Kollidon VA64	BASF Ltd, Mumbai
Plasdone K29/32	Ashland India Pvt Ltd.
HPMC- E4	Ashland India Pvt Ltd.
HPMC-AS	Ashland India Pvt Ltd.
Klucel LF	Ashland India Pvt Ltd.
Soluplus	BASF Ltd, Mumbai
Methanol	Merck Laboratories
Dichloromethane	Merck Laboratories
Cross Carmellose Sodium	Candila Pharmaceuticals Ltd.
Lactose	Candila Pharmaceuticals Ltd.
Empty Hard gelatine Capsules	Astron Research Ltd., Ahmedabad.

3. METHOD:

Solid Dispersion Method:

Rivaroxaban is a BCS Class II drug hence, it has a poor solubility due to this to achieve the enhanced solubility of the API the Solid dispersion method is used. The concept of solid dispersion was coined by Sekiguchi and Obi. This term refers to at least two components usually a hydrophilic matrix and hydrophobic drug. The commonly used hydrophilic carriers like polyethylene glycol(PEG), polyvinylpyrrolidone(PVP).

Various technique is used to prepare solid dispersion which are as follows:

Fusion method 2) Solvent Evaporation method 3)Spray Drying

Solvent Evaporation Method:

The solid dispersion is prepared by using carriers like kollidon VA-64, soluplus, HPMC-AS, plasdone , klucel, methocel HPMC in ratio as follows10ml of solvent (5ml dichloromethane+ 5ml methanol) was taken in volumetric flask dissolve the drug slowly until it turns turbid. And with the help of Sonicator this dispersion made soluble and clear. Further 125 of drug was soluble in 10ml solvent (5ml dichloromethane+5ml methanol).

Added same amount of polymer to this solution to make it 1:1 solid dispersion. Similarly with the help of above procedure 125mg of drug is taken with 62.5mg of polymer to make mixture of 1: 0.5 ratio solid dispersion Again same procedure was applied to make 1:1.5 SD the 125 mg of Rivaroxaban taken and the 187.5 mg of polymer taken that would make solid dispersion of 1:1.5 The above mixture of.

Drug and polymer were added in petri dish and set for the evaporation of solvent for 24 hours. At 60^0C temperature in Hot Air Oven. After the evaporation process, solid dispersion then scrapped out of petri dish with help of spatula . and this powder is triturate using mortal pastel to make uniform SD. This solid Dispersion then weighed and percentage yield was calculated. Solid dispersion prepared with different polymers and different ratio are as follows.

Table2: Ratio of different carrier in solid dispersion

Sr. No.	API + Carrier	Ratio		
1	API+ Soluplus	1:0.5	1:1	1:1.5
2	API+ KollidonVA-64	1:0.5	1:1	1:1.5

3	API+ HPMC-AS	1:0.5	1:1	1:1.5
4	API+ PlasdoneK30	1:0.5	1:1	1:1.5
5	API+ Klucel	1:0.5	1:1	1:1.5
6	API+ Methocel HPMC	1:0.5	1:1	1:1.5

Fig 2: Preparation of Solid Dispersion

Method of Formulation of Different Batches: Rivaroxaban 2.5mg was weighed and filled in the capsule firstly for the comparative dissolution study. The API (Rivaroxaban) is thoroughly mixed with the super disintegrants, and then other excipients are added to the mixer and passed through the sieve no 40 . collect the powder mixer, blend with lactose and subject the blend for capsule filling. The screening of polymer and optimised ratio was done with the help of solubility study analysis using UV Spectrophotometer.

Table 3: Formulation of Different batches

Sr No	API: Polymer	API: Polymer (Quantity)	Lactose (mg)	Cross Carmellose Sodium(mg)	Total (mg)
1	API: Kollidon (1:0.5)	2.5:1.25=3.75	88.25	8	100
2	API: Kollidon (1:1)	2.5:2.5=5	87	8	100
3	API: Kollidon (1:1.5)	2.5:3.75=6.25	85.75	8	100
4	API: Soluplus (1:0.5)	2.5:1.25=3.75	88.25	8	100
5	API: Soluplus (1:1)	2.5:2.5=5	87	8	100
6	API: Soluplus (1:1.5)	2.5:3.75=6.25	85.75	8	100
7	API: HPMC-AS (1:0.5)	2.5:1.25=3.75	88.25	8	100
8	API: HPMC-AS (1:1)	2.5:2.5=5	87	8	100
9	API: HPMC-AS (1:1.5)	2.5:3.75=6.25	85.75	8	100

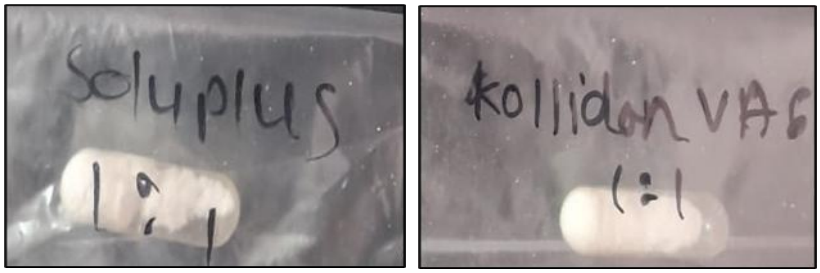


Fig 3: Prepared capsules

4. RESULT AND DISCUSSION:

Calibration curve of Rivaroxaban:

Preparation of First stock solution:(0.1mg/ml or 100ug/ml)

Weighing accurately 10mg of drug add dissolve in 10ml Solvent (dichloromethane) i.e. pre add dissolve properly and this is first stock .

Preparation of second stock solution and Dilutions:

Remove 1ml from the stock solution and dilute upto the 10ml this is the second stock solution and then aliquots are taken from the second stock solution take 1ml and dilute upto 10ml (0.1ug/ml), 2ml dilute upto 10ml (0.2ug/ml), 3ml dilute upto 10ml (0.3ug/ml) and so on .

Table4: standard calibration curve in DCM

Sr No	Concentration (ug/ml)	Absorbance
1	0.1	0.034
2	0.2	0.058
3	0.3	0.078
4	0.4	0.104
5	0.5	0.117

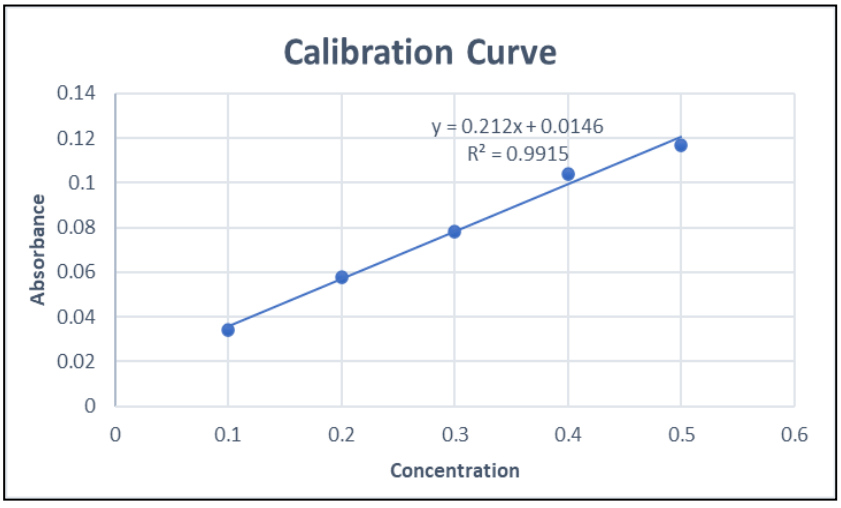


Fig 4: Standard calibration curve in DCM

In this investigation, analytical method obeyed beer-lambert law in the concentration range 0.1-0.5 ug/ml and it was suitable for the estimation of rivaroxaban using phosphate buffer. The value of correlation coefficient (r^2) for the linear equation was found to be more than 0.99 which Indicates a positive correlation between the concentration between the concentration of drug and corresponding absorbance values.

Table 5: Calibration Curve result

Sr. No.	Parameters	Observations
1	Lambda max	251nm
2	Regression Equation	Y=0.212x
3	Correlation Coefficient(r^2)	R^2=0.9915

DRUG-EXCIPIENT COMPATIBILITY STUDY:

Fourier Transform Infrared Spectroscopy (FTIR):

The interaction between Rivaroxaban and carrier was confirmed by obtaining infrared spectra for Rivaroxaban and solid dispersion with carrier from an FTIR spectrophotometer (Model: IR Affinity- IS, A219652, Shimadzu, Japan). This mixture was then introduced in the sample holder and scanned between the wavelength ranges of 4500 to 250 cm. Each sample analysis included 45 scans, at a resolution of 4 cm-1. depicts the FTIR spectra of rivaroxaban and solid dispersion with carrier like soluplus, kollidonVA64, PalsdoneK30, methocel HPMC-LV, klucel, HPMC-AS etc.

1] FTIR Spectra Of Rivaroxaban

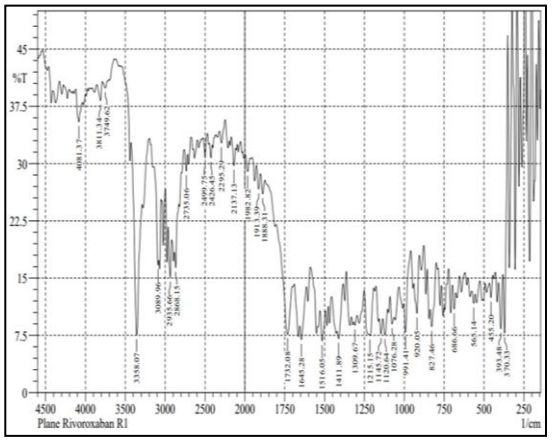


Fig 5: FTIR Spectra of API

3] FTIR Spectra of SD with Kollidon

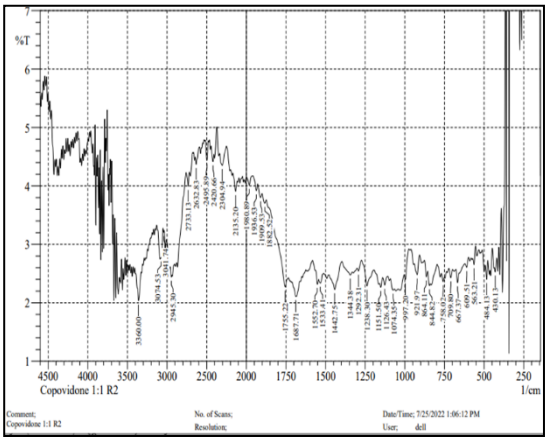


Fig 6:FTIR Spectra of Batch R2

2] FTIR Spectra of SD with Soluplus

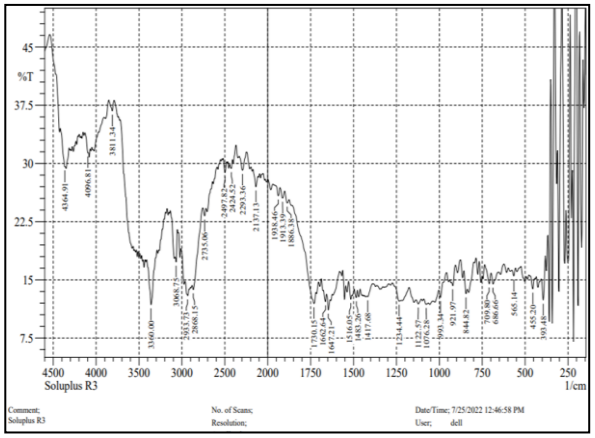


Fig 7: FTIR Spectra of Batch R1

4] FTIR Spectra of SD with HPMC-AS

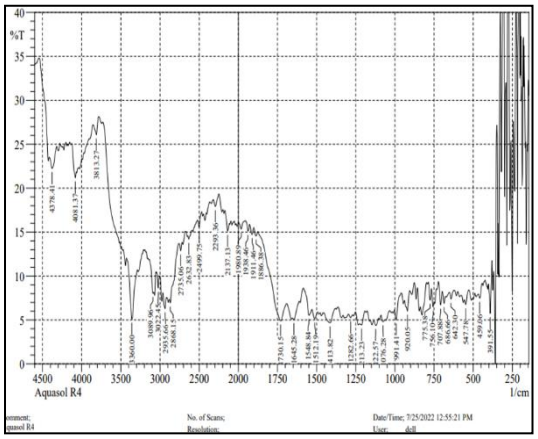


Fig 8: FTIR Spectra of Batch R3

Table 6 : Interpretation of Rivaroxaban by FTIR

Sr No.	Functional group	Standard Frequency Range	Frequencies(cm^{-1})

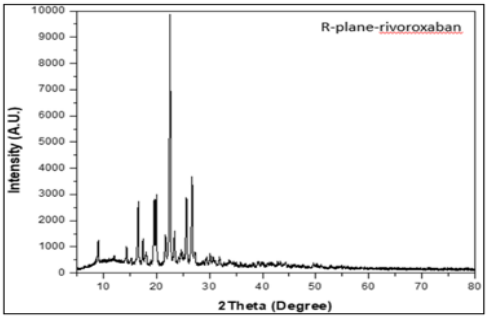
			Pure Drug	R1	R2	R3
1	N-H Stretching (aliphatic)	3300-3400	3358.07	3360	3360	3360
2	C-H Stretching (aliphatic)	3000-3100	3089.96	3068.75	3074.53	3022.45
3	C=O Stretching (aliphatic)	1700-1750	1732.08	1730.15	1755.22	1730.15
4	C=C Stretching (aromatic)	1500-1550	1516.05	1516.05	1533.41	1512.19
5	C-N Stretching (aliphatic)	1000-1300	1076.28	1076.28	1074.35	1076.28
6	Benzene Stretching	700-800	827.46	709.80	709.80	707.88

X-RAY DIFFRACTION STUDIES:

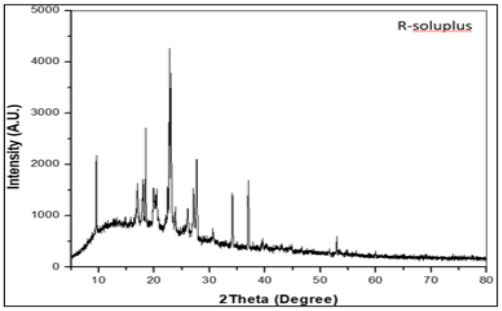
The crystallinity of Rivaroxaban and solid dispersion with the carrier like soluplus, kollidone, HPMC-AS, Plasdone, klucel, Methocel Hpmc were evaluated using a powder X-ray diffractometer. The samples were scanned with the diffraction angle increasing from 10^0 to 80°. The Figure represents X-ray diffractograms of Rivaroxaban and solid dispersion with carrier like soluplus, kollidoneVA64, HPMC-AS, PlasdoneK30, methocel HPMC-LV, klucel.

The diffraction of the Rivaroxaban exhibits characteristics sharp crystalline peaks at 25°, 26.5^0. 27^0, 24.5^0, 20^0, 17^0,16^0, 14^0, $10.^0$ In comparison to the Solid Dispersion, the diffractogram of the Rivaroxaban revealed the disappearance of most of the crystalline peaks associated with the Polymers; however, the diffractogram of Solid dispersion with polymer like in case of HPMC-AS, Methocel-HPMC showed a broad, fused peak with reduced intensity, which is characteristic of the amorphous. The disappearance of crystalline peaks of Of Rivaroxaban showed the formation of solid dispersion with polymer. In solid dispersion XRD pattern the picks are disappeared in comparison to the pure rivaroxaban and thus the crystalline nature is replaced with the amorphous form. Less intense peaks are showing the Amorphous nature.

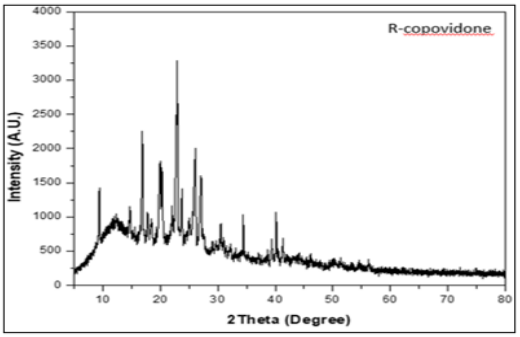
1.X-Ray Diffraction Pattern of Rivaroxaban: 2.XRD Of SD with Soluplus:



Fig·9:·XRD·of·API



Fig·10:·XRD·of·SD·with·soluplus¶



Fig·11:·XRD·Of·SD·With·KollidonVA64

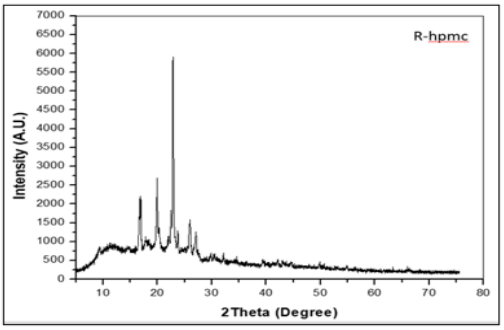


Fig12:·XRD·of·SD·with·HPMC-AS¶

DIFFERENTIAL SCANNING CALORIMETRY:

The aim of this study is to investigate the drug–excipient compatibility between rivaroxaban tablet and pharmaceutical excipients by a combination of thermal and spectroscopic methods. In DSC analysis the endothermic peak shows the melting in which the heat is supplied and in the exothermic peak shows the crystallinity and starting peak shows the glass transition state.

In DSC analysis the endothermic peak shows the melting in which the heat is supplied and in the exothermic peak shows the crystallinity and starting peak shows the glass transition state. Melting of Solid Dispersion takes place at the nearly same temperature at which the pure rivaroxaban melt(melting Point 230^{0}C).

Sample	Endothermic Peak [Melting]	Heat [mJ]
Rivaroxaban	232.68	-31.45
Soluplus	231.42	-13.43
KollidonVA64	226.37	-35.42

1] Differential scanning calorimetry analysis of rivaroxaban:

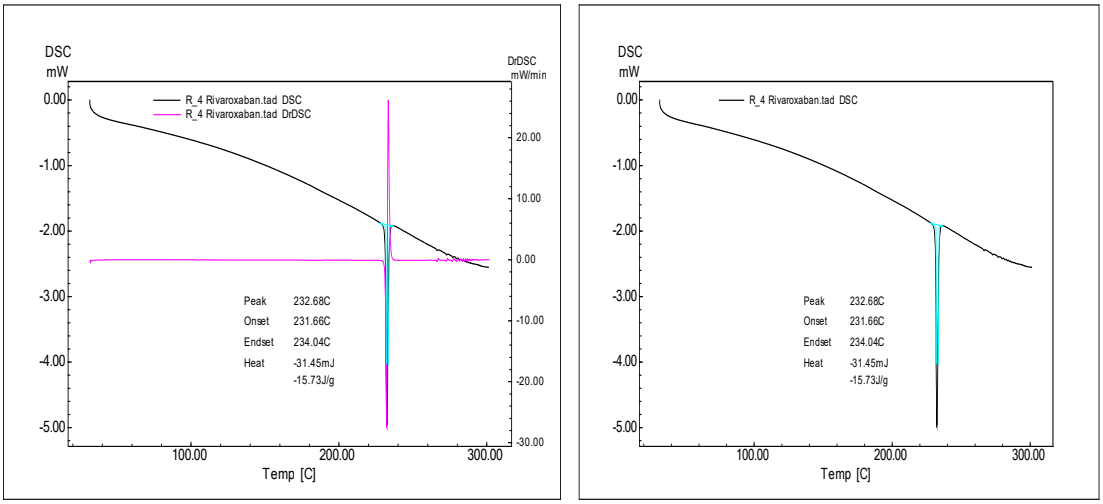


Fig 13: DSC analysis of Rivaroxaban

2] Differential scanning calorimetry analysis of Solid Dispersion with Soluplus:

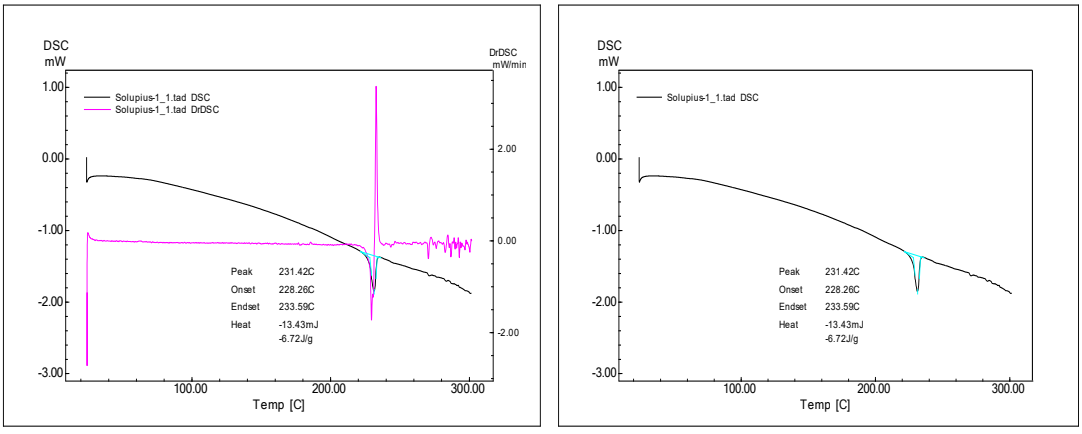
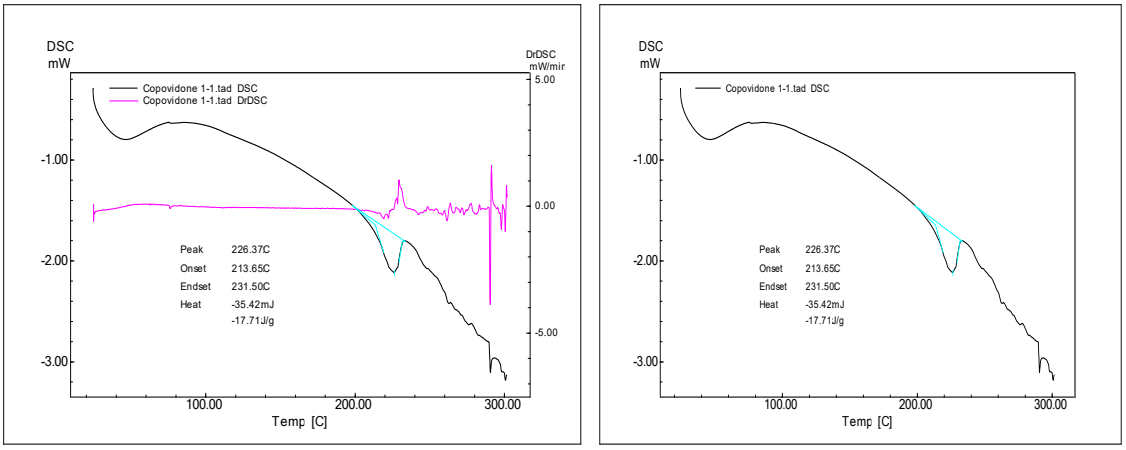


Fig 14: DSC analysis of SD with Soluplus

3] Differential scanning calorimetry analysis of Solid Dispersion with Kollidon:



SCANNING ELECTRON MICROSCOPY RESULT:

1] API [Rivaroxaban

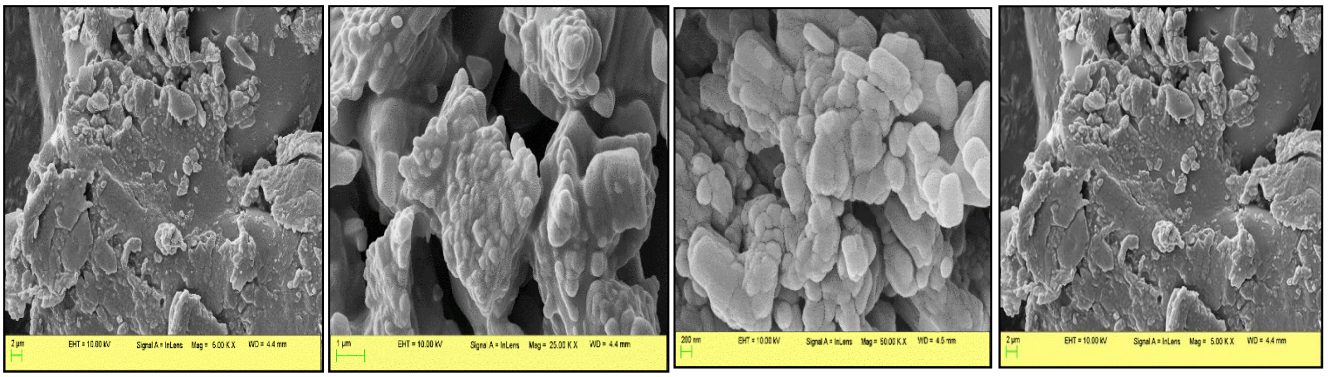


Fig 15: SEM result of Rivaroxaban

2] SEM Result of Solid Dispersion with Soluplus:

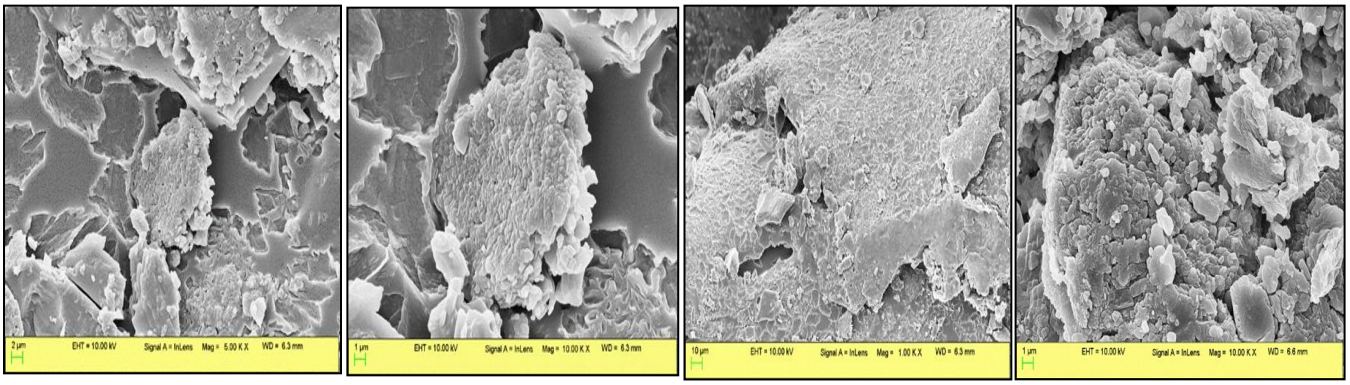


Fig16: SEM result of Solid Dispersion with soluplus

3] SEM of Solid Dispersion with KollidonVA64:

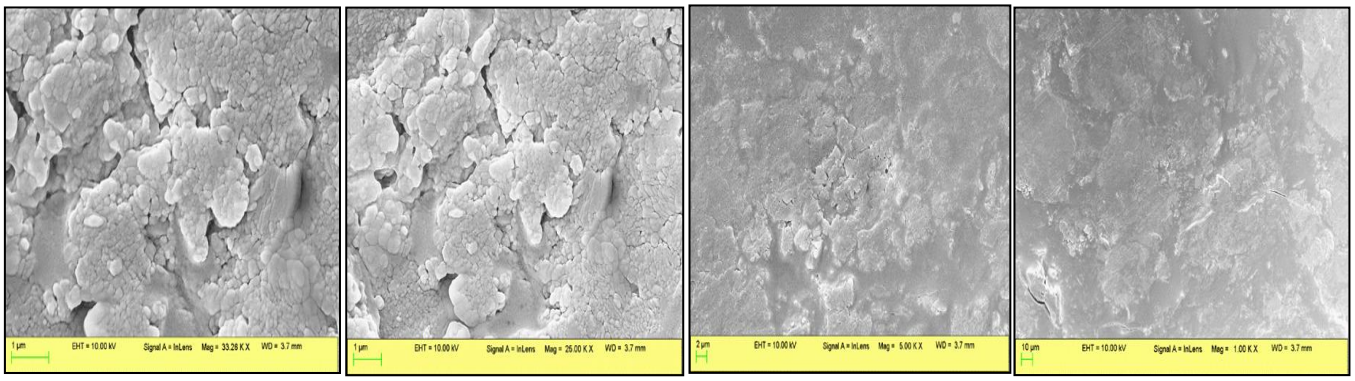


Fig17: SEM result of solid dispersion with KollidonVA64

SEM of the solid dispersion reveals irregular particles with several microscopic cracks and crevices, which provides additional surface for deposition of the drug particles. There is no evidence of drug crystals, which confirms the previous findings on PXRD and thermogram patterns. The SEM images also revealed that the particles exhibited large sub angular irregular shaped morphology with smooth surface. Surface morphology of the solulpus, kollidon is shown in above fig.

DETERMINATION OF SOLUBILITY OF SOLID DISPERSION

The solid dispersion prepared with different carriers in 1:0.5, 1:1, 1:1.5 ratio was carried out and evaluated for solubility, the rivaroxaban with soluplus shows hights solubility, and with KollidonVA64 than others carrier like PlasdoneK30, klucel, HPMC-AS as shown in below table Solid dispersion are prepared with different carrier in three different ratios and this dispersion placed in various buffer solutions like 6.8 phosphate buffer, 4.5 acetate buffer,0.1 NHCL, and water and kept for 24 hr and then filter the solution and check the solubility of the solution by the uv spectrophotometer.

On the basis of the below result the solubility of rivaroxaban is better with the polymer kollidone and soluplus with respect to the other polymers in solid dispersion.

Solvent	Rivaroxaban	API:Kollidon			API:Plasdone			API:Klucel		
		1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5
Phosphate Buffer(6.8)	0.43	0.53	1.34	0.94	3.32	2.57	4.73	0.53	1.45	0.52
Acetate Buffer(4.5)	1.23	2.94	2.15	1.8	3.87	1.58	1.70	3.2	1.40	1.58
0.1N HCL	0.56	1.88	1.17	5.56	1.96	2.10	2.14	1.62	1.61	0.87
Water	0.51	0.51	3.46	3.32	3.6	4.6	5.82	3.36	4.42	2.00

Solvent	Rivaroxaban	API:HPMC-AS			API:HPMC-LV			API:Soluplus		
		1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5
Phosphate Buffer(6.8)	0.43	1.66	4.12	1.81	0.73	0.53	0.35	1.78	5.34	3,75
Acetate	1.23	1.15	3.22	1.15	1.99	9.96	1.77	1.28	6.87	1.17

Buffer(4.5)										
0.1N HCL	0.56	1.60	1.78	1.09	1.90	11.89	4.69	1.09	3.95	2.63
Water	0.51	7.43	9.2	8.2	3.35	11.96	2.88	2.15	1.05	0.78

Table 7:Interpretation of Solubility Study

Solvent	Phosphate Buffer (6.8)			Acetate buffer (4.5)			0.1N HCL			Water		
Rivaroxaban Solubility	1.43			1.23			0.56			1.51		
Folds of increase in solubility after SD	1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5	1:0.5	1:1	1:1.5
Soluplus	1.24	3.73	2.62	1.04	1.52	0.95	1.94	6.96	4.69	4.21	2.0	1.52
KollidonVA64	1.06	0.93	1.12	2.39	1.74	1.46	3.35	2.08	9.92	1.19	6.78	6.5
HPMC-AS	1.16	2.88	1.26	0.93	2.61	1.09	2.85	3.17	1.94	14.6	18	16
PlasdoneK30	2.32	1.91	3.30	3.14	1.28	1.38	3.5	3.75	3.82	7	9	11.4
KlucelLF	-	1.01	-	2.6	1.1	1.3	2.89	2.8	1.5	6.6	8.6	3.92
HPMC-LV	-	-	-	1.6	8.09	1.4	3.3	21	8.8	6.5	23	5.6

Soluplus, HPMC-AS shows the maximum folds of increase in solubility in 6.8 Phosphate buffer in ratio 1:1, hence soluplus, Aquasol with ratio 1:1 is more suitable for formulation of optimized batch and which is summarized are as follows.

From the above study we find the More suitable Polymer and Ratio for final batches:

SD with Ratio (1:1)	Solubility	Folds of Increase in Solubility as compared with API	% Increase in solubility as compared to API
Rivaroxaban(API)	1.43	1	100%
SD with Soluplus	5.34	3.73	373.4%
SD with HPMC-AS	4.12	2.88	288.11%
SD with kollidonVA64	1.34	0.93	93.70%

Solubility of pure Rivaroxaban drug substance in pH 6.8 Phosphate Buffer media is 1.43ug/ml, while after Preparing Solid Dispersion with Soluplus solubility increase in 3.73 folds as compared to the pure rivaroxaban and % increase in solubility is 373.4% . In case of Solid dispersion with HPMC-AS in 6.8 phosphate buffer with ratio 1:1 the solubility increases 2.88

folds and the % increase in solubility was found to be 288.11% as compare to the rivaroxaban having solubility 1.43. However there were no improvement in solubility with KollidonVA64 Solid Dispersion.

The solid dispersion prepared with different carriers in 1:0.5, 1:1, 1:1.5 ratio was carried out and evaluated for solubility, the rivaroxaban with soluplus shows highest solubility, and others carrier like PlasdoneK30, KlucelLF, HPMC-LV as shown in above table.

Solid dispersion is prepared with different carrier in three different ratios and this dispersion placed in various buffer solutions like 6.8 phosphate buffer, 4.5 acetate buffer, 0.1 NHCL, and water and kept for 24 hr and then filter the solution and check the solubility of the solution by the UV spectrophotometer. On the basis of the above result the solubility of rivaroxaban is better with the polymer kollidone and soluplus with respect to the other polymers in solid dispersion.

INVITRO DISSOLUTION OF OPTIMIZED BATCHES OF CAPSULE:

Pure API (5mg) was filled in the capsule undergo dissolution under the above dissolution condition and then after the specific time period like 10, 15, 30, 45, 60, 90, 120 min, 5ml of sample withdrawn from the dissolution media and this sample undergo solubility study with the help of spectrophotometer and then the % drug release calculated which are as follows.

The formulation of rivaroxaban capsule which contain 2.5mg drug(API) in three different ratio 1:0.5, 1:1, 1:1.5 with carrier like soluplus, kollidone,HPMC-AS and other excipient undergo dissolution and the % drug release from these batches are as follows. 5ml of sample withdrawn at predetermined time interval of 10, 15 ,30 ,45 ,60 ,90, and 120 min. The withdrawn samples were analysed by UV spectrophotometer at 251nm using phosphate buffer as blank.

Table 8: General dissolution condition

Sr.No.	Parameter	Specifications
1	Dissolution medium	pH 6.8 phosphate buffer+ 0.2% sodium lauryl sulphate
2	Temperature	37+_0.5^{0}C
3	Rotation speed	100rpm
4	USP Type I	Basket
5	Volume withdrawn	5ml
6	Lambda max	251 nm

1]Percentage drug release of drug from Pure Drug(Rivaroxaban):

Time	Abs	Conc	Conc of drug in 900ml	Cumulative conc of drug	Conc of drug in mg	% DR
0	0	0	0	0	0	0
10	0.039	0.13	117	117	0.117	2.34
15	0.054	0.2	180	297	0.297	5.94
30	0.07	0.27	243	540	0.54	10.8
45	0.172	0.73	657	1197	1.19	23.8
60	0.204	0.88	792	1989	1.98	39.6
90	0.278	1.12	1008	2997	2.99	59.8
120	0.342	1.5	1350	4347	4.3	86

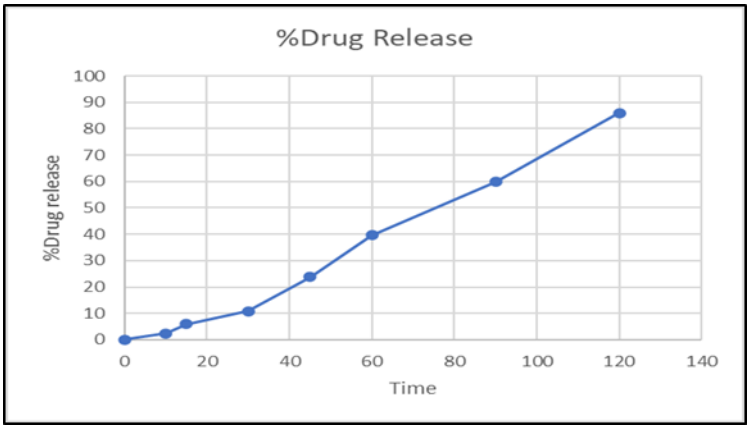


Fig 18:% DR from API

1] %Drug Release from Solid Dispersion with soluplus batch R1

Time	Soluplus %DR [1:0.5]	Soluplus % DR [1:1]	Soluplus % DR[1:1.5]
10	5.04	5.76	4.8
15	10.8	13.68	14.04
30	18.36	22.32	25.92
45	29.88	32.8	39.6
60	43.2	46.08	54.72
90	62	66.6	71.64
120	88	99.72	103.6

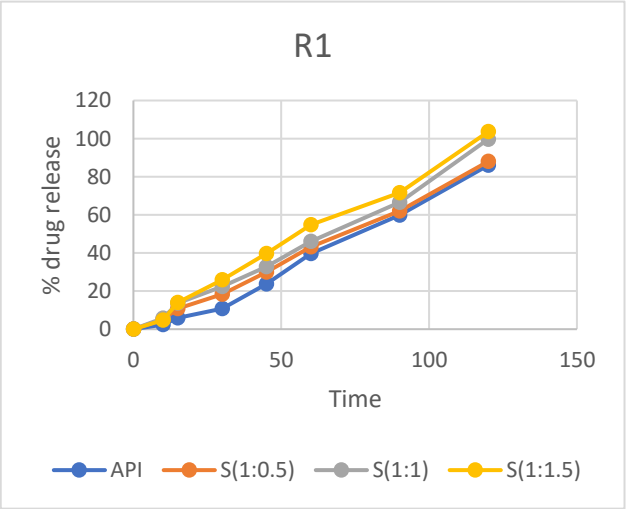


Fig 19: %DR from batch R1

2] % Drug Release from Solid Dispersion With KollidonVA64 Batch R2

Time	Kollidon[R2] % DR [1:0.5]	Kollidon[R2] % DR [1:1]	Kollidon[R2] % DR [1:1.5]
10	5.6	3.6	3.16
15	12.4	12.96	8
30	20.4	25.2	15.6
45	32	38.8	27.6
60	46	54.36	41.6
90	62.8	70.56	58.4
120	82	92.8	76.8

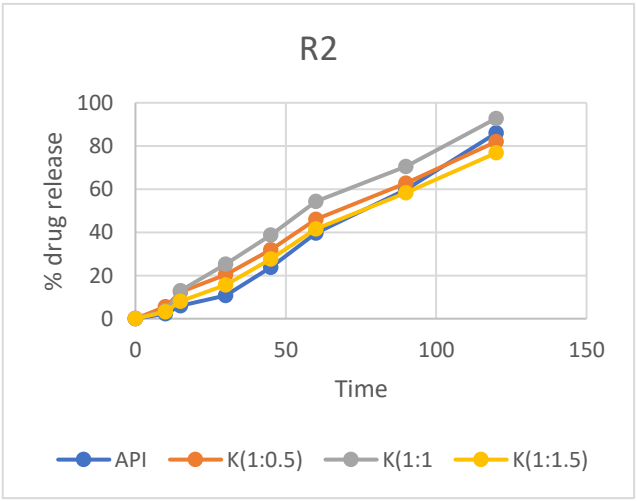


Fig 20: %DR from batch R2

3] % Drug Release From Solid Dispersion with HPMC-AS Batch R3

Time (min)	HPMC-AS %DR(1:0.5)	HPMC-AS %DR (1:1)	HPMC-AS %DR(1:1.5)
10	2.32	1.36	0.72
15	5.16	4.84	2.4
30	9.48	9	4.72
45	15.24	13.96	8.68
60	23.16	20.72	13.6
90	32.16	29.44	22.36
120	50	40.4	32.08

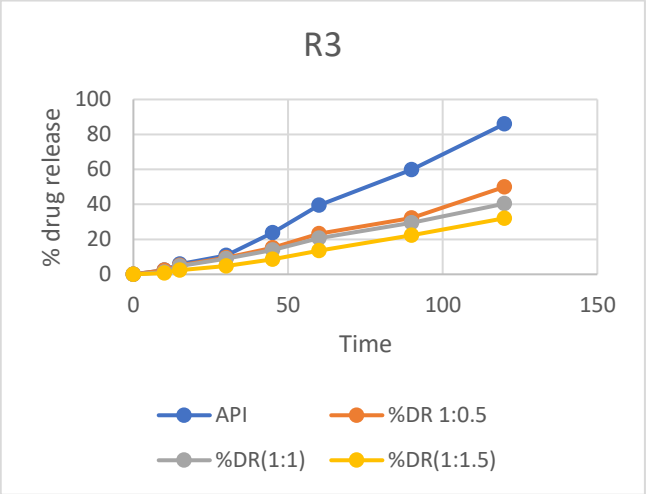


Fig 21:%DR from batch R3

4] % Drug Release From Marketed Preparation of Rivaroxaban

Time	Rivaroxaban % DR [T1]	Rivaroxaban % DR [T2]	Rivaroxaban % DR [T3]
10	14.04	11.52	12.6
15	29.16	24.84	27.72
20	47.16	39.24	49.5
30	67.68	60.48	64.08
45	96.12	90	93.96

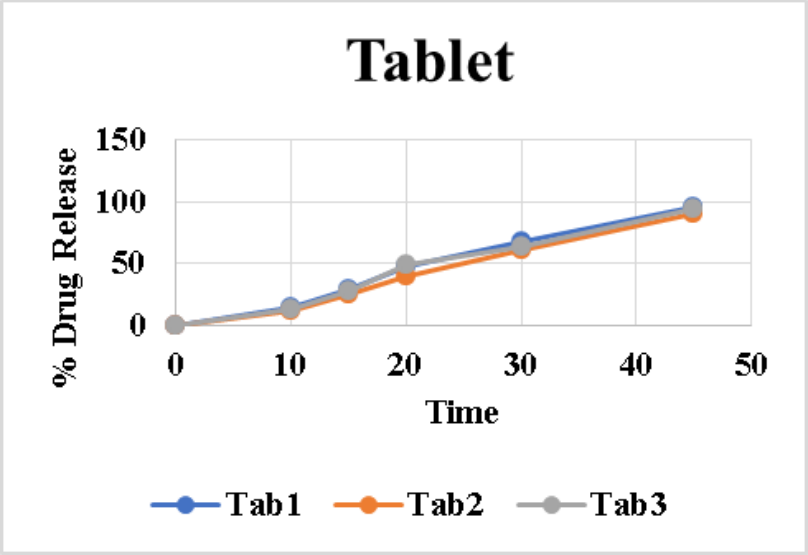


Fig 22:% DR from marketed preparation

SUMMARY

The aim of the present study was to enhance the solubility of pH sensitive drug like Rivaroxaban by solid dispersion method

and formulation and evaluation of rivaroxaban capsule with the help of different carriers. And increases the solubility of the drug which is having the low solubility.

The Work Done Is Summarized as Follows:

By enhancing solubility of rivaroxaban by solid dispersion using different carriers like soluplus, kollidoneVA64, HPMC-AS, PlasdoneK30, HPMC-LV, Klucel with the three different ratios like 1:0.5, 1:1, 1:1.5 . Flow properties such as angle of repose, bulk density ,tapped density are evaluated and shows good flow property. Evaluation of the final dosage form was done by dissolution study and % drug release was found to be satisfactory.

The Drug-Polymer compatibility study was done with the help FTIR, X-ray diffraction, Scanning Electron microscopy and Differential scanning calorimetry and result of all this are satisfactory.

Standard calibration curve was prepared to determine the drug concentration in final prepared formulation of Rivaroxaban. And UV analysis was done the determine the % drug release from dissolution study.

5. CONCLUSION:

The present study was aimed to formulate the Ph sensitive drug with the help of solid dispersion method. In this study the formulation of rivaroxaban capsule by the solid dispersion with the help of different polymers was done. And this formulation was done in three different ratios like 1:0.5, 1:1, 1:1.5.

From the Result and discussion, it is concluded that although the rivaroxaban belongs to the BCS Class II drug Hence it has low solubility we can increase the solubility of rivaroxaban with the help of the solid dispersion method which is prepared by the solvent evaporation method can increase solubility in folds than that of the pure rivaroxaban.

From the above study we find the More suitable Polymer and Ratio for final batches:

SD with Ratio (1:1)	Solubility	Folds of Increase in Solubility as compared with API	% Increase in solubility as compared to API
Rivaroxaban(API)	1.43	1	100%
SD with Soluplus	5.34	3.73	373.4%
SD with HPMC-AS	4.12	2.88	288.11%
SD with kollidonVA64	1.34	0.93	93.70%

From the above result it is conclude that the after preparation of solid dispersion solubility increase in folds as compared to the pure rivaroxaban. In case of Solid dispersion with soluplus in 6.8 phosphate buffer with ratio 1:1 the solubility increases 3.73 folds and % increase in solubility was found to be 373 as compare to the rivaroxaban having solubility 1.43. and another polymer shows increase in solubility after solid dispersion was HPMC-AS in 6.8 phosphate buffer with ratio 1:1, the 2.88 folds and % increase in solubility was found to be 288 as compare to Rivaroxaban having solubility 1.43. However there were no improvement in solubility with KollidonVA64 Solid Dispersion.

Soluplus, HPMC-AS shows the maximum folds of increase in solubility in 6.8 Phosphate buffer in ratio 1:1, hence soluplus, HPMC-AS with ratio 1:1 is more suitable for formulation of optimized batch.

Drug polymer compatibility study was studied with the help of various studies like X-Ray Diffraction which shows the amorphous preparation of solid dispersion which form has more solubility than that of the crystalline form, Differential Scanning Calorimetry, FTIR Which shows the functional group present in the rivaroxaban and solid dispersion the result shows that the both present the same functional groups.

Finally, the Evaluation the final dosage form was done with the help of the Dissolution study by calculating the % drug release from the dosage form. % Drug release from Dosage form was good. And the finally formed dosage form is having good solubility, stable dissolution study profile.

FUTURE SCOPE OF THE STUDY:

Further the formulation containing the prescribed quantities of the selected ingredients may be suggested for the in vivo and clinical evaluation. Further the formulation may prove to be enhancing the patient treated with Venous Thromboembolism.

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CONFLICT OF INTREST:

None

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