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SOLUBILITY ENHANCEMENT OF ANTIVIRAL DRUG-ACYCLOVIR BY SOLID DISPERSION TECHNIQUE

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Abstract:
The objective of present study was to improve the dissolution rate of Acyclovir. The major drawback of Acyclovir is its low aqueous solubility that delays its absorption and has poor oral bioavailability (15-30%). Solubility was increased by solid dispersion technique using a water soluble carrier, Kollidon VA64 (VA64), Soluplus (SOL) and Eudragit EPO (EPO). The solid dispersions were prepared by solvent evaporation method. The prepared solid dispersions showed an enhancement in dissolution rate and solubility compared to API. In vitro release profiles of all SDs were comparatively evaluated. Faster dissolution was exhibited by solid dispersion containing 1:4 ratio of drug: Eudragit EPO. The prepared solid dispersion was subjected for % practical yield, drug content, infrared (IR) spectroscopic, differential scanning calorimetry (DSC). FT-IR spectra and DSC revealed no chemical incompatibility between drug and polymer. The solid dispersion in drug: Eudragit EPO (1:4, w/w) was relatively stable at 40 °C/75% RH conditions for at least 3 month.

Key words: *Solid dispersions, carriers, solubility enhancement, poorly soluble drugs, bioavailability*

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INTRODUCTION

Therapeutic effectiveness of a drug depends upon the bioavailability and ultimately upon the solubility of drug molecules. Solubility behavior of a drug is one of the key determinants of its oral bioavailability. In recent years, the number of poorly soluble drug candidates has increased tremendously. There are various techniques available to improve the solubility of poorly soluble drugs such as Micronization, Nanosuspension, Modification of the crystal habits, Eutectic mixtures, Solid dispersions, Micro emulsions, Self micro emulsifying drug delivery systems, cyclodextrin inclusion and lipid based delivery systems etc [1, 2]. Solid dispersion is one of these methods, which was most widely and successfully applied to improve the solubility, dissolution rates and consequently the bioavailability of poorly soluble drugs. The concept of solid dispersions (SDs) was introduced in 1961 by Sekiguchi [3, 4] in which the drug is dispersed in inert water - soluble carrier at solid state. Several water soluble carriers such as mannitol, urea, lactose, citric acid, polyvinyl pyrrolidone (PVP) and polyethylene glycols are used as carriers for SDs [4-7].

Acyclovir is a purine nucleoside (deoxiguanosine) analogue, has activity against human herpes viruses. One of the most commonly used antiviral drugs; it is primarily used for the treatment of herpes simplex virus infections, as well as in the treatment of herpes zoster. Acyclovir was seen as the start of a new era in antiviral therapy, as it is extremely selective and low in cytotoxicity. The major drawback of this drug is its low aqueous solubility that delays its absorption and has poor oral bioavailability (15-30%), hence intravenous administration is necessary if high concentrations are required. When orally administered, peak plasma concentration occurs after 1–2 hours.

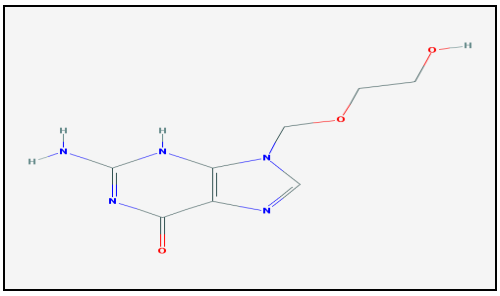

Fig 1: Structure of Acyclovir

Soluplus is used as a solubilizer in oral and parenteral formulations and has been shown to enhance dissolution of poorly water soluble drugs from solid dosage forms. Eudragit EPO is used as a plain or insulating film former; it is soluble in gastric fluid below PH 5.0. Copovidone is used widely in pharmaceutical formulations and is generally regarded as nontoxic. It has no irritating or sensitizing effects on the skin. So these polymers can be used for preparation of solid dispersions [8].

The present study is aimed to formulate solid dispersion of acyclovir to overcome its low bioavailability by preparing solid dispersion with various water soluble polymers such as Kollidon VA64 (VA64), Soluplus (SOL) and Eudragit EPO (EPO).

MATERIALS AND METHOD

Materials

Acyclovir was obtained as a gift sample from Mylan laboratories, Hyderabad. Kollidon VA64 (VA64), Soluplus (SOL) and Eudragit EPO (EPO) of pharmacopoeial grade were obtained from Lupin Research Park, Aurangabad. All reagents were of A.R. grade. Double distilled water was used for all the experiments.

Characterization Study of Drug

The drug sample (Acyclovir) was analyzed for physical appearance and powder nature. Melting point of acyclovir was determined by taking a small amount of sample in a capillary tube closed at one end and placed in Digital melting point apparatus. The melting point was noted. The UV spectrum of Acyclovir was obtained using UV-Visible Spectrophotometer (Schimadzu). The IR spectra of drug sample were recorded by using KBr pellet method. The thermal behavior of Acyclovir was studied using Shimadzu DSC TA60 WS Thermal Analyzer. The solubility of acyclovir in distilled water was determined [12,13].

Preformulation Study of Acyclovir

Parameters like bulk density, tapped density, Carr's index, Hausner's ratio, angle of repose of drug were determined [11].

Analytical Method Development

The calibration curve in water and 0.1 N HCl was prepared by plotting absorbance versus concentration of Acyclovir.

The stock solution was prepared by accurately weighing 10 mg of the drug, dissolved in sufficient quantity of distilled water and 0.1 N HCl and the volume made upto 100 ml [11,12].

Different aliquots were taken from stock solution and diluted with distilled water and 0.1 N HCl separately to prepare series of concentrations from 5-25 µg/ml. Absorbance was measured at λmax against distilled water as blank on a UV-Visible Spectrophotometer. absorbance versus concentration of Acyclovir [12].

Table 1: Composition of Solid Dispersion

Sr.No	Composition	Batch	Ratio
1	Acyclovir:soluplus	A1	**1:1 (w/w)**
2	Acyclovir:soluplus	A2	**1:2 (w/w)**
3	Acyclovir:soluplus	A3	**1:3 (w/w)**
4	Acyclovir:soluplus	A4	**1:4 (w/w)**
5	Acyclovir:soluplus	A5	**1:5 (w/w)**
6	Acyclovir:kollidon VA64	B1	**1:1 (w/w)**
7	Acyclovir:kollidon VA64	B2	**1:2 (w/w)**
8	Acyclovir:kollidon VA64	B3	**1:3 (w/w)**
9	Acyclovir:kollidon VA64	B4	**1:4 (w/w)**
10	Acyclovir:kollidon VA64	B5	**1:5 (w/w)**
11	Acyclovir:Eudragit	C1	**1:1 (w/w)**
12	Acyclovir:Eudragit	C2	**1:2 (w/w)**
13	Acyclovir:Eudragit	C3	**1:3 (w/w)**
14	Acyclovir:Eudragit	C4	**1:4 (w/w)**
15	**Acyclovir:Eudragit**	**C5**	**1:5 (w/w)**

Validation Parameters of Method for Acyclovir in Distilled Water and 0.1 N HCl

The Validation of analytical method was performed as per ICH guidelines.

Preparation of Solid Dispersions

Acyclovir and the various polymers were weighed in different ratio. Accurately weighed quantity of polymers in various 1:1, 1:2, 1:3, 1:4, 1:5 (drug: carrier) proportion were carefully transferred into glass flask and dissolved in Methanol. To these solutions, accurately weighed quantities of Acyclovir were added and allowed to dissolve. Then solvent was removed by evaporation by stirring at magnetic stirrer at 40^0 c for 1hr. The obtained residue was dried for 2 hrs and stored in desiccators overnight. Next day the dried residue was grinded in mortar and sieved trough mesh # 60 [11, 12].

Evaluation of Acyclovir Solid Dispersions

Aqueous Solubility Study

The solubility of Acyclovir as pure drug and its solid dispersion were determined in distilled water. Acyclovir and solid dispersion of drug was taken and to this 10 ml of respective medium was being added in 100 ml stoppered volumetric flask and shaken for 25 hrs at RT on magnetic stirrer. The entire samples were protected from light by wrapping the flask by aluminum foil. After 24 hr samples were filtered through Whatman filter paper no. 42 and aliquots were suitably diluted and assayed spectroscopically at 252 nm. Solubility was determined in triplicate and average values were reported [13].

***In-vitro* Dissolution Studies**

Dissolution study of pure drug and its solid dispersion was carried out by using paddal type dissolution apparatus for 1 hr. the stirring rate was 50 rpm. The dissolution medium was 900 ml 0.1 N HCL kept at 37°C ± 0.5°C. The solid dispersions containing 200 mg equivalent of Acyclovir was added in the dissolution apparatus. Samples of 5 ml were withdrawn at specified time intervals, filtered and analyzed spectrophotometrically at 252 nm using UV-visible spectrophotometer. The samples withdrawn were replaced by fresh 0.1N HCL solution. Each preparation was tested in triplicate and then means values were drug release and the same was used while plotting the release curves. The percent drug release at various time intervals calculated and plotted against time. The values were calculated for cumulative % drug release and the same was used while plotting the release curves [14].

Drug Content

The solid dispersions of drug prepared by solvent evaporation method were assayed for drug content by dissolving specific amount of solid dispersions in 10 ml of distilled water. The solutions were filtered and were further diluted such that the absorbance falls within the range of standard curve. The absorbances of solutions were determined at 252 nm by UV-visible spectrophotometer. Three replicates were prepared and average value was reported [13].

FTIR Spectroscopic Study

The FTIR spectra of the drug, Eudragit polymer and solid dispersion in 1:4 ratios were recorded with FTIR spectrophotometer. The sample were prepared by the using potassium bromide and scanned for absorbance 4000-400 cm^{-1}.

Differential Scanning Calorimetry

DSC pattern of drug, Eudragit polymer and solid dispersion in 1:4 ratios were recorded using Schimadzu DSC instrument

Powder X-ray diffractometry

X-ray diffraction measurements of the solid dispersions were performed on a Diffractometer system=XPERT-PRO, jagtar at Panjab University.

Stability Study

Stability study for selected solid dispersions was carried out by storing 1 gm of solid dispersions in an amber colored screw capped bottle at different temperatures and relative humidity, accelerated (40 ± 2°C/75 ± 5 % RH) and Room temperature for a period of 3 months. Samples are withdrawn at 0, 15, 30 and 60 days periods. These samples were visually examined for percent drug content and *In-vitro* dissolution study [14].

RESULTS AND DISCUSSION

Characterization test of Drug

The drug Acyclovir was found to be white in color and crystalline in nature which complies with the reported. The average melting point of Acyclovir was determined by capillary method and was found to be 257^0c, which is in good agreement with reported melting point.

UV Spectra

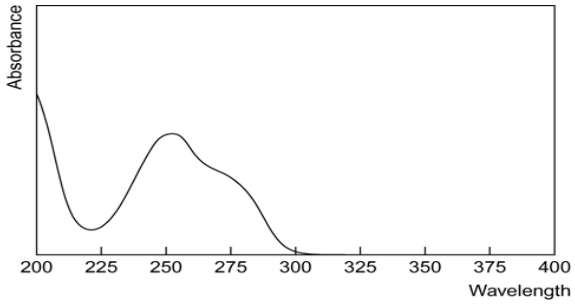

Fig 2: UV spectrum of Acyclovir

The UV spectrum of Acyclovir was obtained using UV-Visible Spectrophotometer in the range 200 to 400 nm. The λ_{max} was found to be 252 nm which complies with the reported [15].

Infra-Red Spectra

The IR spectra of drug sample were recorded by using KBr pellet method. The spectrum obtained was concordant with the reference[38] as depicted in Table 2 and Figure 3. Hence Acyclovir was identified by IR Spectroscopy.

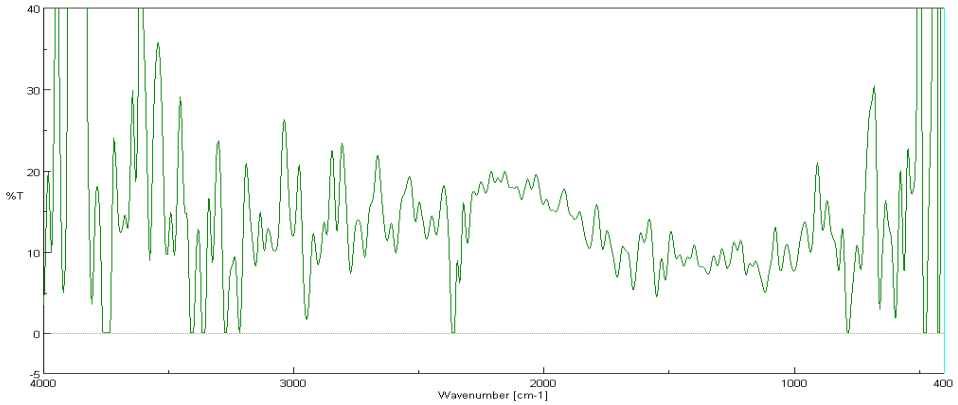

Fig 3: IR spectra of Acyclovir

Table 2: Interpretation of IR Spectra of Acyclovir

SR. No.	Wavenumber (cm^{-1})	Functional group present
1	3575.38	O-H stretching
2	1114.65	C-O stretching
3	3478.95	Primary N-H stretching
4	2946.7	aliphatic C-H stretching
5	1704.76	C=O Stretching

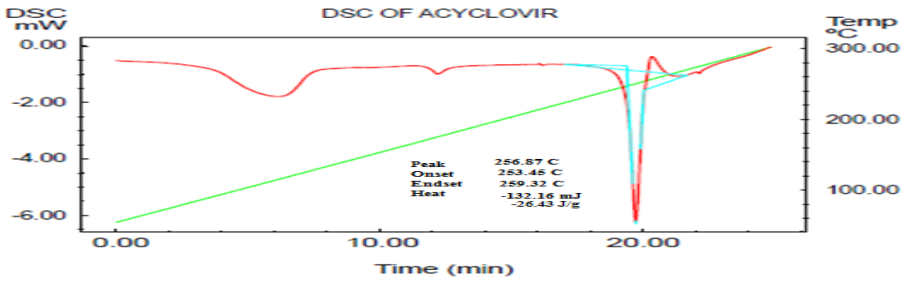

Fig 4: DSC thermogram of Acyclovir

Differential Scanning Calorimetry (DSC)

The DSC thermogram was recorded and it shows one endothermic peak maximum of 256.87°C. This was in accordance with the reported [14]. Hence Acyclovir was identified by DSC shown in figure 4.

On the basis of melting point, UV spectrum, Infrared spectrum and DSC thermogram, the procured sample of Acyclovir was found to be of acceptable purity and quality. The sample was taken for further studies.

Solubility

The solubility of acyclovir in distilled water was found to be 1.03mg/ml. The reported value for solubility of Acyclovir in water is 1.3 mg/mL at 25 °C and in 0.1N HCl solubility was found to be 1.14 mg/ml as according to literature Acyclovir dissolves in dilute hydrochloric acid [17].

Preformulation Study of Acyclovir:

Standard procedures are followed to obtain the flow properties of drug and the obtained results are as shown in table no 3.

The bulk density and tapped density of granules or powder are important parameters in the compressibility of the granules or powder. The bulk density was 0.62 gm/cm^3 and tapped density was found 0.76 gm/cm^3. The Hausner's ratio is another parameter indicating the flow properties. It was found to be 1.23. The value of ratio below 1.25 indicates good while above 1.25 indicates the poor flow. The Carr's index is indicator of compressibility. It was found to be 62.5 %. The values below 20 % shows good compressibility and above it show poor compressibility. The angle of repose 20 to 30º indicates the good flow while the angle of repose more 30º indicates poor flow properties and angle of repose below 20º indicates excellent flow properties. The angle of repose was found 58^0 indicating poor flow ability.

According to the results obtained it is concluded that, Acyclovir has poor flow shown in table 3.

Analytical Method Development:

The UV spectrophotometric method was selected for estimation of Acyclovir. The UV spectrum exhibited maximum absorbance (λ_{max}) at 252 in distilled water. The standard calibration curve exhibited good coefficient of correlation as shown in Table 4.

Table 3: Preformulation parameters for Acyclovir

Sr.No	Parameter	Observed	Flow property
1	Bulk Density	0.62g/cc	----
2.	Tapped Density	0.76g/cc	----
3.	Carr's index	62.5%	Poor
4.	Hausners ratio	1.23	Good
5.	Angle of Repose	58^0	Poor

Table 4: Standard calibration curve of Acyclovir in Distilled Water

Conc.(µg/ml)	Absorbance
5	0.337
10	0.662
15	0.954
20	1.24
25	1.523

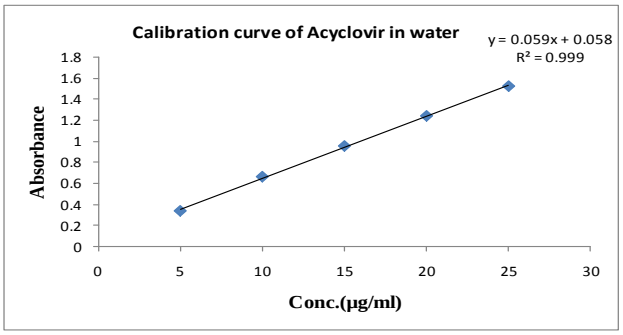

Fig 5: Standard Calibration Curve of Acyclovir in Distilled Water

The UV spectrum exhibited maximum absorbance (λmax) at 255 in 0.1 N HCl. The standard calibration curve exhibited good coefficient of correlation as shown in Table 5.

Table 5: Standard Calibration Curve of Acyclovir in 0.1 N HCl

Conc.(µg/ml)	Absorbance
5	0.342
10	0.662
15	0.942
20	1.302
25	1.609

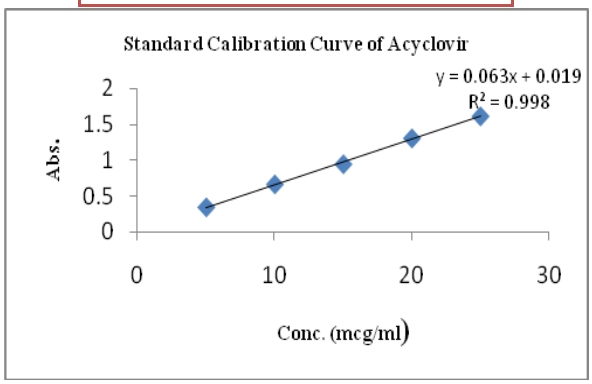

Fig 6: Standard Calibration Curve of Acyclovir in 0.1 N HCl

Validation Parameters of method for Acyclovir in distilled water:

Developed method was validated and validation parameters are listed in Table 6.

Table 6: Validation Parameters

Parameter	Limit	Results
Accuracy	98 - 102	100.03% ±1.808
Repeatability	%RSD < 2	0.0851%
Intraday precision	%RSD < 2	0.284%
Inter day precision	%RSD < 2	0.554%
Linearity	R^2 > 0.9997 %	0.999
Range	-	5-25µ/ml
LOD	-	0.08836 µ/ml
LOQ	-	0.2677 µ/ml

From the above result, it is seen that all the values of parameters evaluated are within the limits given by ICH guidelines. So the developed UV spectroscopic method for Acyclovir is accurate, precise and specific.

Formulation of Preliminary Batch

Acyclovir and the various polymers Solid dispersions were prepared by solvent evaporation method.

Solubility

Solubility was determined in triplicate and average values were reported in Table 7. From the solubility data it was found that solid dispersion prepared using soluplus, Kolidon VA64 and Eudragit EPO in the proportion of 1:4 has good solubility as compared to other drug polymer ratio. It can be concluded that saturation level was reached at ratio 1:4 in all batches. So for further study the solid dispersion of A4, B4, C4 batches were selected and evaluated.

Evaluation of Acyclovir Solid Dispersions

Table 7: Solubility of Acyclovir from Various Solid Dispersions

S.N.	Solid dispersions	Solubility in distilled water (mg/mL)
1	API	**1.03 ±1.30**
2	A1	**1.39 ±1.93**
3	A2	**1.47 ±1.42**
4	A3	**1.48 ±1.48**
5	A4	**1.64 ±2.36**
6	A5	**1.59 ±1.54**
7	B1	**1.22 ±2.51**
8	B2	**1.32 ± 1.65**
9	B3	**1.40 ± 1.39**
10	B4	**1.74 ± 1.48**
11	B5	**1.55 ± 2.36**
12	C1	**1.5 ±1.51**
13	C2	**1.6 ±1.93**
14	C3	**1.8 ±1.90**
15	C4	**2.7 ± 1.36**
16	**C5**	**2.4 ±1.33**

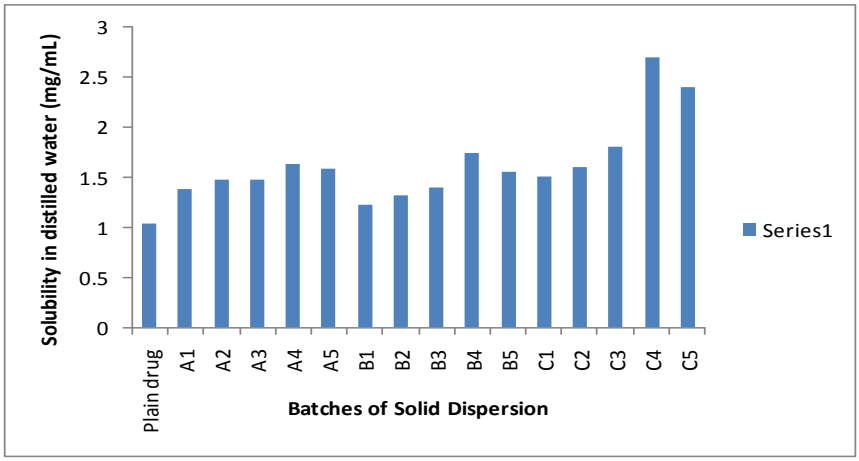

Fig 7: Solubility of Acyclovir from Various Solid Dispersions

Table 8: Flow properties of Solid Dispersion C4 batch

Sr.No	Parameter	Observed	Flow property
1	Bulk Density	0.468g/cc	----
2.	Tapped Density	0.578g/cc	----
3.	Carr's index	26.8%	Poor
4.	Hausners ratio	1.22	Good
5.	Angle of Repose	28.85^0	Passable

Powder Characteristics

The solid dispersion of C4 batch was evaluated for bulk density, tapped density, Carr's index (compressibility), angle of repose and Hausner's ratio. Standard procedures are followed to obtain the flow properties of solid dispersion & the obtained results are as shown in table 8.

The Hausner's ratio was found to be 1.22. The value of ratio below 1.25 indicates good while above 1.25 indicates the poor flow. The Carr's index was found to be 26.8%. The values below 20 % shows good compressibility and above it show poor compressibility. The angle of repose was found to be 28.85^0, indicates good flow ability. According to the results obtained it is concluded that, Solid dispersion has good flow as compared to API.

Drug Content

The percent drug content of solid dispersion were determined using powder equivalent to 20 mg of Acyclovir and was dissolved in minimum amount of methanol and volume was made up to mark 100 mL using 0.1N HCl.

The drug content of different solid dispersion is as shown in **Table 9.**

Table 9: Drug content of solid dispersion

S.N.	Composition	Drug content (%)
1	Acyclovir:Soluplus (1:4)	82.139 ± 1.48
2	Acyclovir:kollidon (1:4)	90.37± 1.75
3	Acyclovir:Eudragit (1:4)	100.93± 1.30

Dissolution Studies

The dissolution studies on pure drug, solid dispersions and marketed tablet were performed. Cumulative percent drug dissolved upto one hour was found out at each time interval and graph was plotted between cumulative % drug dissolved and time in min. shown in Fig 8.

Table 1: Percent Drug Release of Acyclovir in 0.1 N HCl

Sr. No.	Time (min)	Percent Drug release				
		API	Marketed Tablet	A4 (1:4)	B4 (1:4)	C4 (1:4)
1	0	0	0	0	0	0
2	10	39.25 ±1.39	71.39 ±1.58	56.27 ±2.36	61.53 ±3.69	71.34 ±1.46
3	20	44.52 ±1.08	78.10 ±1.72	61.38 ±1.56	65.90 ±2.15	86.62 ±2.68
4	30	50.23 ±1.78	79.01 ±1.11	62.51 ±2.43	69.43 ±1.23	90.23 ±2.43
5	40	52.43 ±1.19	80.44 ±1.12	64.99 ±2.04	69.55 ±1.21	94.22 ±2.73
6	50	52.67 ±1.28	81.85 ±1.16	67.90 ±1.06	74.47 ±2.75	97.70 ±1.63
7	60	53.03 ±1.21	83.16 ±1.22	70.70 ±1.89	77.45 ±1.54	97.92 ±1.31

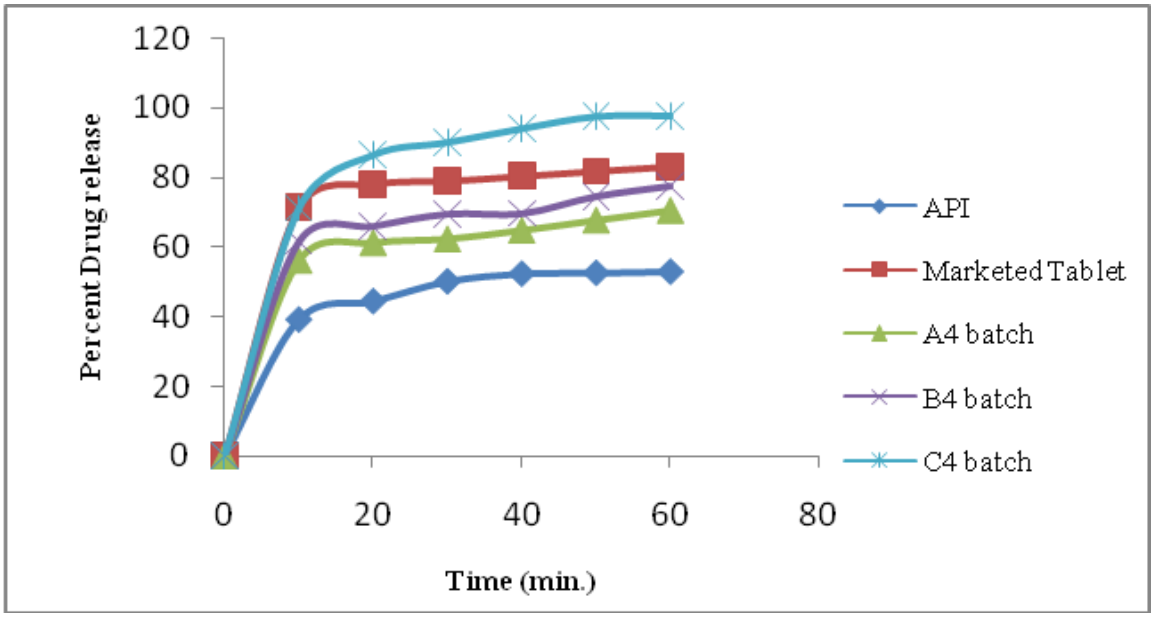

Fig 8: Dissolution Profile of Acyclovir, Marketed Tablets and Solid Dispersion Prepared using Soluplus, Kollidon and Eudragit in 0.1 N HCl

Drug Content

The percent drug content of solid dispersion were determined using powder equivalent to 20 mg of Acyclovir and was dissolved in minimum amount of methanol and volume was made up to mark 100 mL using 0.1N HCL.

The drug content of different solid dispersion is as shown in **Table 11.**

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FTIR Spectroscopic Study

The FTIR spectra of the drug and Eudragit polymer solid dispersion in 1:4 ratios were recorded with FTIR spectrophotometer, as shown in figure 9. The sample of solid dispersion was prepared by the using potassium bromide and scanned for absorbance 4000-400 cm $^{-1}$.

From the FTIR spectra of Acyclovir, Eudragit and solid dispersion of Acyclovir and Eudragit in, it was found that there is no functional group change when acyclovir reacts with Eudragit. So they are found to be compatible.

Differential Scanning Calorimetry

The DSC thermograms of Eudragit and Acyclovir: Eudragit are shown in figure 10 and 11 respectively. When we compare thermograms the peaks of drug and eudragit are retained in DSC of solid dispersion. Hence we can conclude that drug has retained its thermal properties in solid dispersion.

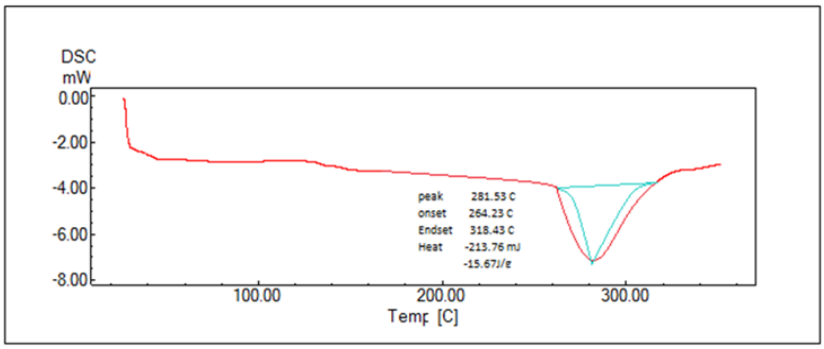

Fig 10: DSC Thermogram of Eudragit

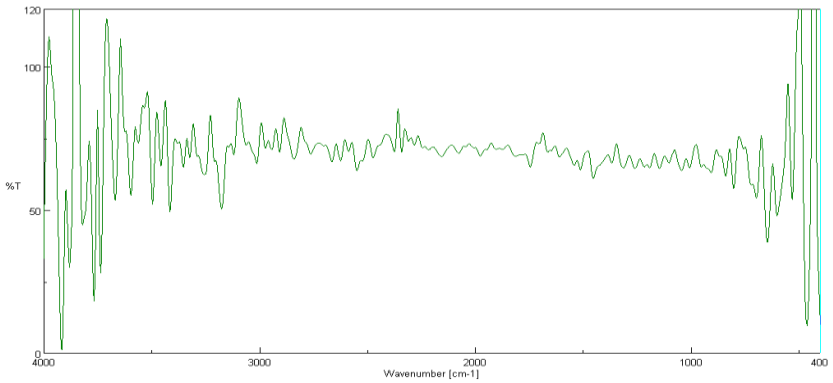

Fig 9: FTIR Spectra of Solid dispersion of Acyclovir and Eudragit (1:4)

Table 12: Interpretation of FTIR of Solid Dispersion

SR. No.	Wavenumber (cm^{-1})	Functional group present
1	3563.81	O-H stretching
2	1145.51	C-O stretching
3	2958.27	aliphatic C-H stretching
4	1743.33	C=O stretching

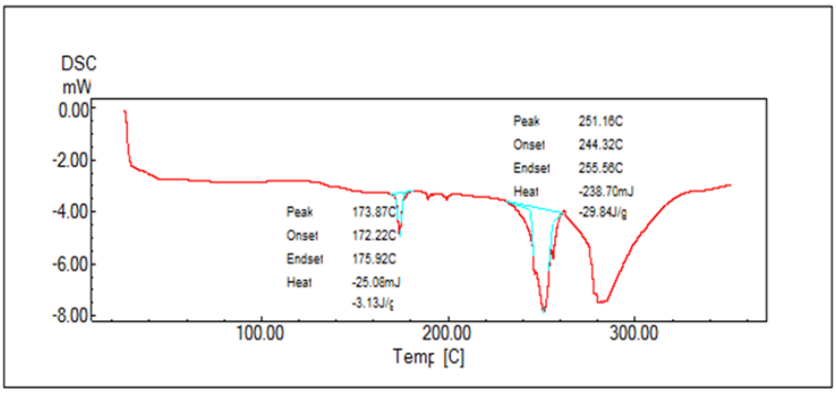

Fig 11: DSC Thermogram of Acyclovir+Eudragit Solid Dispersion

Powder X-ray Diffractometry

X-ray diffractogram of Acyclovir and Acyclovir-Eudragit solid dispersion are shown in Figure no 12 and 13. The diffraction pattern of the pure Acyclovir showed it's highly crystalline nature, as indicated by the numerous distinctive peaks with major characteristic diffraction peaks appearing at a diffraction angle of 2θ at 7.24^0, 12.18°and 25.70°.
The diffraction pattern of Acyclovir-Eudragit solid dispersion shows the peaks of Acyclovir with reduction in peak intensities indicating that the conversion of crystalline form to partial amorphous state.

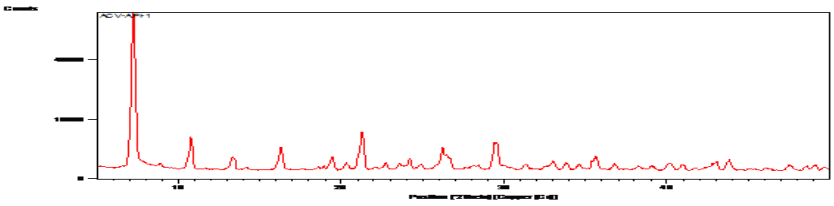

Fig 12: XRD Thermogram of Acyclovir

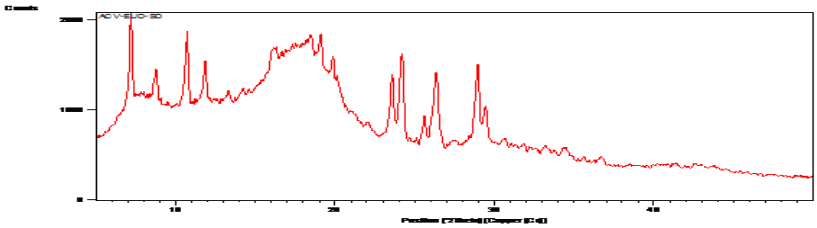

Fig 13: XRD Thermogram of Acyclovir+Eudragit Solid Dispersion

Stability Studies

The solid dispersion C4 containing Acyclovir:Eudragit (1:4) subjected to accelerated stability studies according to ICH guidelines. These studies were carried out by investigating the effect of temperature on the physical appearance of the solid dispersion, percent drug content and drug release from the fast solid dispersion.

Table 13: Physical appearance of solid dispersion during stability study

Parameters	Time (in days)			
	00	30	60	90
Physical Appearance	White	White	White	White

There was no significance changes occur in physical appearance as shown in table 13. The results thus indicated that there were no visible and physical changes observed in the solid dispersion after storage.

Drug content of Solid Dispersion (C4) during Storage

The drug content was found above 98.36%, 99.88% at 40 ±2°C/75 ± 5% RH and room temp respectively, at the end of three months. This indicates that solid dispersion is fairly stable at storage condition as there were no significant changes observed in the drug content. The results of drug content study are reported in table 14.

Table 14: Drug Content of solid dispersion (C4) Stored at Varying Temperature and 75± 5% R.H.

Days	Solid dispersion (C4)	
	25ºC ± 2ºC	40ºC ± 2ºC
0	100.93±0.05	99.04±2.05
15	100.45±1.03	99.23±1.50
30	100.17±0.55	98.4±2.60
45	100.04±0.78	97.65±1.78
60	99.88±0.62	98.36±1.85
90	99.56±1.82	97.38±1.64

*Represents mean ± S.D. (n = 3)

Percent Drug Release for Three Months

It was also observed that there was no significant change in the drug release patterns from these tablets. The results for dissolution of C4 solid dispersion (Acyclovir:Eudragit in the ratio 1:4) are shown in table 15. When Paired t test was applied P value 0.4423 was obtained which is greater than 0.05, shows that the initial percent drug release and percent drug release are not significantly different.

Table 15: Percent Drug Release

Time (min.)	Percent drug release							
	Zero days		After 30 days		After 60 days		After 90 days	
	Room Temp.	40^{0}C ±2 ^{0}C, RH 75±5%	Room Temp.	40^{0}C ±2^{0}C, RH 75±5%	Room Temp.	40^{0}C ±2^{0}C, RH 75±5%	Room Temp.	40^{0}C ±2^{0}C, RH 75±5%
0	0	0	0	0	0	0	0	0
10	71.34	71.35	77.98	75.91	73.57	73.85	74.40	74.28
20	86.63	86.63	85.12	84.59	84.44	83.33	81.32	81.42
30	90.23	90.23	90.07	90.91	90.56	87.73	87.87	87.58
40	94.22	94.22	95.06	95.66	95.94	94.99	94.63	95.44
50	97.71	97.71	95.65	97.85	96.99	95.92	95.94	96.28
60	97.92	97.96	97.85	97.72	97.83	97.52	97.57	97.47

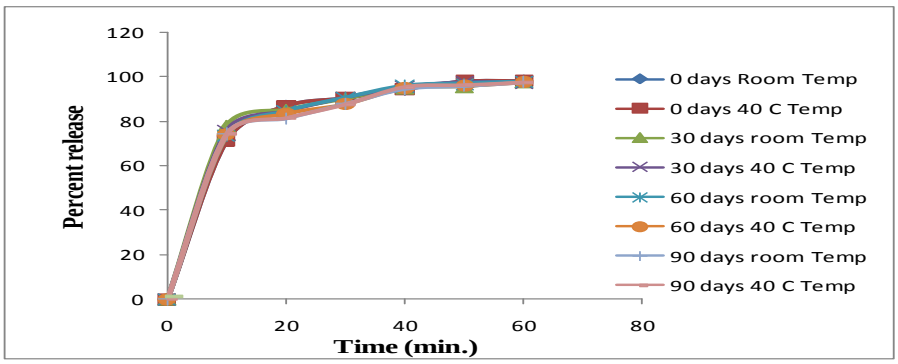

Fig 1: Percent Drug Release Profile for Solid Dispersion of Acyclovir and Eudragit (1:4) for Three Months

Table 16: Statistical t-test for Stability Study

Room temp	Zero Days	90 days	40^0C ±20C, RH 75±5%	Zero Days	90 days
Mean	89.6750	86.8320	**Mean**	89.6833	87.0000
SD	9.9895	9.0799	**SD**	9.9924	9.3625
SEM	4.0782	4.0607	**SEM**	4.0794	4.1870

Statistical t-test for Stability Study:

The two-tailed P value equals to 0.4423 and 0.5125 at 95% confidence interval for four degrees of freedom for drug release at room temperature study and 40^0C ±2^0C, RH 75±5% for 3 months. By conventional criteria, this difference is considered to be not statistically significant. The results are reported in table 16.Hence it can be concluded that solid dispersion was quite stable at storage conditions for stability study.

CONCLUSION

Solid dispersions of drug were prepared by using different polymers. The solid dispersions were prepared by Solvent evaporation method. Various solid dispersions were prepared using Soluplus, Kollidon VA64 and Eudragit in 1:1, 1:2, 1:3, 1:4 and 1:5 w/w ratios for initial optimization of polymer. The % drug content of all solid dispersions were determined by using powder equivalent to 200 mg of Acyclovir and drug content of all solid dispersion were in the range of 81-101%. The dissolution data of API in 0.1 N HCl showed that the highest release of drug is less than 53.03 % in 60 minutes, and thus it can be concluded that Acyclovir is poorly soluble drug and also possess several dissolution related problem and that might be a reason for its poor bioavailability. The solubility and dissolution results revealed that there was an increase in solubility and dissolution of all the solid dispersions as compared to pure drug. The FTIR and DSC of the solid dispersion of Acyclovir and Eudragit show that all the peaks of drug and Eudragit are as it is and drug is present in free form. Hence no interaction between them was observed. A result of stability study indicated that the solid dispersion (C4) was stable and there was no significant changes observed in the drug content. Finally, it may be concluded that solid dispersion prepared by solvent evaporation method with Eudragit showed good promising dissolution and solubility enhancement property.

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