European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 07, Issue 02, 2020

Original research article

Study of Preformulation Parameters of Ganciclovir (GCR) for the Preparation of Solid Dispersion

Lokendra Singh Chundawat [1], Dr. Chatan Singh Chouhan [2]

[1]Ph D scholar, Bhupal Nobles' Institute of Pharmaceutical Sciences, B. N. University, Udaipur, Rajasthan, India.

[2]Professor & HOD, Bhupal Nobles' Institute of Pharmaceutical Sciences, B. N. University, Udaipur, Rajasthan, India.

Corresponding Author: Lokendra Singh Chundawat

Abstract

Aim: The aim of the present study is to study the Preformulation parameters of Ganciclovir (GCR) for the preparation of SDs of GCR was prepared by microwave fusion method in upcoming study.

Material & Methods: Preformulation study i.e. solubility, assay, melting point, drug excipient compatibility study, DSC, FT-IR and various parameters for pre compression of flow property were measured.

Results: The Organoleptic properties of pure Ganciclovir (GCR) were physically studied and it was found in the powder form. The color of the drug was found to be white to light yellow with characteristic odour and slightly bitter taste. GCR showed a sharp melting point at 136.5±0.5^{o}C. The solubility of these was found to have solubility <0.3 µg/mL in indicating the very poor solubility of the drugs selected. The Calibration curve for GCR represents slope (y) = 0.0901x+0.0536 with regression (R^2) value of 0.9990, indicates the linearity. The Hygroscopic data of GCR revealed that the drugs are non-hygroscopic as the % weight upsurge was <0.2%. The thermogram of GCR was characterized by single sharp endotherm at 137.29^{o}C (indicates its melting). The DSC thermogram of the drug was observed to be in contract with the specifications.

Conclusion: The main theme behind this research work was to prepare GCR SDs using PEG bases (PEG3350, PEG 4000, PEG6000, PEG8000 and PEG20000), PVP bases (PVP K-12, PVP K-17, PVP K-25, PVP K-30 and PVP K-90), Poloxamers (Poloxamer 108, Poloxamer 188, Poloxamer 237, Poloxamer 338, Poloxamer 407) and Urea.

Keywords: Preformulation parameters, Ganciclovir (GCR), preparation of Solid Dispersion, Poloxamer 108, Poloxamer 188, Poloxamer 237, Poloxamer 338

Introduction

The solid dosage forms (E.g., tablets, capsules) release drug instantly, which are utmost used drug delivery systems (DDS). These dosage forms disintegrate and dissolve gastric fluid.[1] Dissolution of the drug(s) under physiological conditions is vital for its systemic absorption. Dissolution characterization is done for solid orals and to decide the agreement with dissolution necessities when stated in the discrete monograph. [2-3]

With advancement in combinatorial chemistry and high throughput screening large number of drug molecules with required pharmacological activity have been developed.[4] These newly

developed compounds have undesirable physicochemical properties like high lipophilicity, poor aqueous solubility and high molecular weight. The five key physicochemical parameters involved in early compound screening are dissociation constant, solubility, permeability, stability and lipophilicity. Amongst them poor aqueous solubility is ranked higher in the critical compound properties. Dissolution enhancement is thus one of the most important prerequisite in the field of dosage form designing. [5-7]

Till date, various approaches were employed to overcome the limitations of poorly soluble drugs and to enhance their dissolution rates. A very common approach adopted is to enhance the drug release profile of selected drug candidates employing solid dispersion (SDs) by novel microwave fusion practice unlike routine fusion method, hot melt extrusion, solvent evaporation and supercritical fluid practice.[8] The aim of the present study is to study the Preformulation parameters of Ganciclovir for the preparation of SDs of GCR was prepared by microwave fusion method in upcoming study.

MATERIALS AND METHODS

PRE-FORMULATION STUDIES

Melting point
Ganciclovir melting points were determined by an open capillary method. [9]

Saturation solubility
The "descriptive terms" is used to describe the approximate solubility of Pharmaceuticals. The solubility of the drug is an important physicochemical property because it affects the bioavailability of the drug, the rate of drug release into dissolution medium and consequently, the therapeutic efficiency of the pharmaceutical product. [10]
The solubility of GCR in various fluids was determined by the following method. [11]

Analysis of Drug:

Standard Curve for Ganciclovir:

Standard Stock Solution
GCR equivalent to 10 mg was dissolved in 5 mL of 0.1 N HCl in a 10-mL volumetric flask, shaken well and the final volume was adjusted to get a concentration of 1 mg/mL. This 1 mg/mL solution was used as a stock solution.

Calibration Curve
5 mL of 1 mg/mL aliquot solution was further diluted up to 50 mL by 0.1 N HCl in a 100-mL volumetric flask and the final volume was adjusted up to 100 mL. This was scanned spectrophotometrically in the wavelength region 200–800 nm to determine the wavelength of maximum (λ_{max}) absorption. The λ_{max} was found to be 233 nm against blank. From 1 mg/mL stock solution, the serial dilution pattern was followed to obtain aliquots of 0.1–0.5 μg/mL concentration. The calibration curve was plotted between concentration and absorbance. [11]

Hygroscopic studies:
The hygroscopic study of API was done under specified temperature and humidity conditions[12] (i.e. 33%RH, 53%RH & 75%RH).

Drug- Excipient Compatibility Studies:
The compatibility of drugs used (GCR) with the excipient used were tested by Differential Scanning Colorimetry and Fourier Transform Infra-Red Spectrophotometric methods.

Differential Scanning Colorimetry:
Differential Scanning Colorimetry (DSC) of pure drugs and polymers used were studied to investigate any changes in melting points of the drug after combining it with the excipient. DSC curves were obtained by a differential scanning calorimeter (Schimadzu DSC-50, Tokyo, Japan) at a heating rate of 10°C/min from 30°-300°C in the nitrogen atmosphere (20 mL/min) with a sample weight of 3mg.

Fourier Transform Infra-Red spectral analysis:
FTIR spectra of GCR with excipient used were obtained individually and in combinations on an FTIR spectrophotometer, (Perkin Elmer, spectrum-100, Japan) using the KBr disk method (2 mg sample in 200 mg KBr). The spectra were obtained by scanning at 400 to 4000 cm^{-1} with a resolution of 1 cm^{-1}.

Flow properties (Pre Compression)
The solid dispersion blend was tested for the following flow parameters. [13-15]

Angle of Repose (AR):
The frictional forces in loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

Bulk Density:
Both bulk density (BD) and tapped density (TD) were determined. A quantity of 2g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 mL measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-secintervals.

Hausner ratio:
Hausner found that the ratio TD: BD was related to inter particle friction and could be used to predict powder flow properties. Hausner ratio greater than 1.25 is considered to be an indication of poor flow ability.

Table 1: Flow character specifications

Compressibilit Index	Hausner ratio	Flow Character
<10	1.00-1.11	Excellent
11-15	1.12-1.18	Good
16-20	1.19-1.25	Fair
21-25	1.26-1.34	Passable
26-31	1.35-1.45	Poor
32-37	1.46-1.56	Very poor
>38	>1.60	Very very poor

RESULTS

Organoleptic properties of Ganciclovir

The Organoleptic properties of pure Ganciclovir (GCR) were physically studied and it was found in the powder form. The color of the drug was found to be white to light yellow with characteristic odour and slightly bitter taste.

Melting point

GCR showed a sharp melting point at 136.5±0.5^{o}C, as per the literature its melting range is from 134-138^{o}C.

Solubility

The solubility data for pure drugs GCR was tabulated in figure 1.

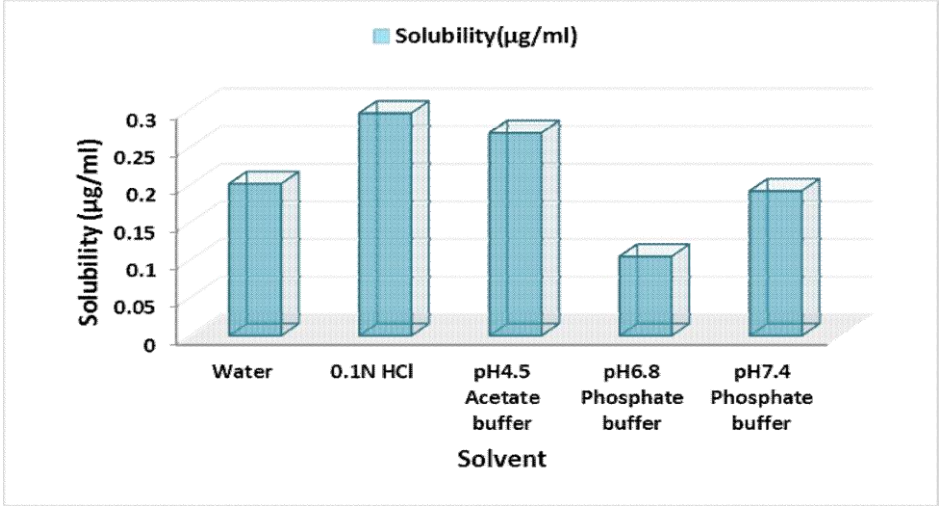

Fig. No. 1: Solubility of Ganciclovir in various solvents

The solubility of these was found to have solubility <0.3 µg/mL in indicating the very poor solubility of the drugs selected.

Analysis of Drugs Used:

The concentration vs absorbance values for the estimation of Ganciclovir was shown in table 2 and the calibration curve was shown in fig. 2.

Table 2: Concentration vs. absorbance values for the estimation of Ganciclovir

Concentration (µg/mL)	Absorbance
2	0.125±0.003
4	0.318±0.001
6	0.473±0.002
8	0.668±0.003
10	0.851±0.002

Values in mean ±SD; trials made (n=3)

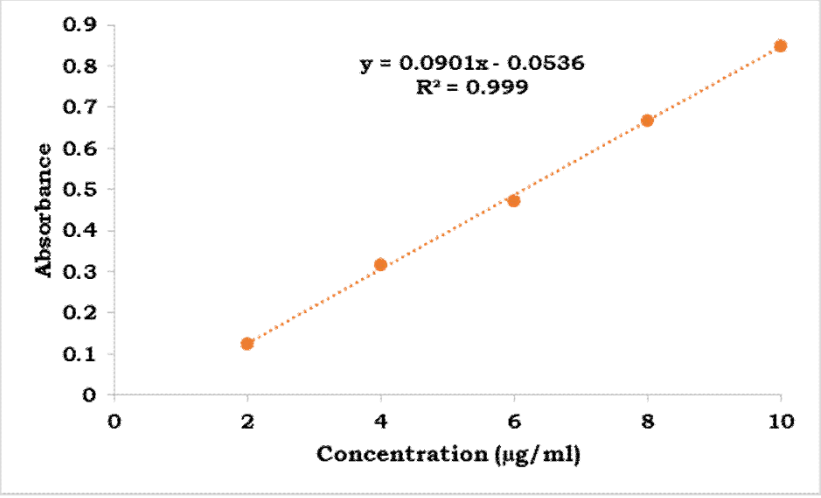

Fig. No. 2: Calibration curve of Ganciclovir

The Calibration curve for GCR represents slope (y) = 0.0901x+0.0536 with regression (R^2) value of 0.9990, indicates the linearity.

Hygroscopic studies:

The hygroscopic data at different humidity conditions were shown in table 3.

Table 3: Hygroscopic Data of Ganciclovir % Weight Change

Time Interval	**33%RH**	**53% RH**	**75% RH**
Day 1	0.00	0.0	0.0
Day 2	0.00	0.01±0.001	0.02
Day 4	0.00	0.01±0.001	0.01±0.001
Equilibrium RH			
Day 0	0.101±0.002	0.102±0.001	0.103±0.001
Day 4	0.113±0.001	0.115±0.003	0.117±0.002

Values in mean ±SD; trials made (n=3)

The Hygroscopic data of GCR revealed that the drugs are non-hygroscopic as the % weight upsurge was <0.2%.

When GCR combined with carriers used in ratios of 1:1 at 40°C and RH of 75% for a period of a month, they retained its white to off white colour and the consistency retained as a powder.

Drug- Excipient Compatibility Studies:

Physical Observations of Excipient Compatibility Study

GCR and Excipient (1:1) compatibility at stressed storage conditions was shown in table 4.

Table 4: Physical Observations of Excipient Compatibility Study

Binary mixture	Initial	Storage condition			
		Room temperature		40°C/75%RH	
		15 Days	30 Days	15 Days	30 Days
GCR	White to off-white powder	NCC	NCC	NCC	NCC
GCR+PEG-3350	White waxy powder	NCC	NCC	NCC	NCC
GCR+PEG-4000	White waxy powder	NCC	NCC	NCC	NCC
GCR+PEG-6000	White waxy powder	NCC	NCC	NCC	NCC
GCR+PEG-8000	White waxy powder	NCC	NCC	NCC	NCC
GCR+PEG-20000	White waxy powder	NCC	NCC	NCC	NCC
GCR+PVP K-12	White to off-white powder	NCC	NCC	NCC	NCC
GCR+PVP K-17	White to off-white powder	NCC	NCC	NCC	NCC
GCR+PVP K-25	White to off-white powder	NCC	NCC	NCC	NCC
GCR+PVP K-30	White to off-white powder	NCC	NCC	NCC	NCC
GCR+PVP K-90	White to off-white powder	NCC	NCC	NCC	NCC
GCR+Poloxamer-108	White to off-white powder	NCC	NCC	NCC	NCC
GCR+Poloxamer-188	White to off-white powder	NCC	NCC	NCC	NCC
GCR+Poloxamer-237	White to off-white powder	NCC	NCC	NCC	NCC
GCR+Poloxamer-338	White to off-white powder	NCC	NCC	NCC	NCC
GCR+Poloxamer-407	White to off-white powder	NCC	NCC	NCC	NCC
GCR+ Urea	White to off-white powder	NCC	NCC	NCC	NCC

GCR= Ganciclovir; PEG=Poly Ethylene Glycol; PVP= Poly Vinyl Pyrrolidone; NCC= No characteristic change

Differential Scanning Calorimetry:

The DSC thermograms of GCR with PEG carrier

The DSC thermograms of Ganciclovir (GCR) with PEG carrier used was shown in tabulated in table 5.

Table 5: Endothermic events, Enthalpy and Inference of DSC data of EPEG

	Endothermic events (°C)				
DSC Fusion Inference sample	**T onset**	**T peak**	**Tend**	**Enthalpy ΔH (J)**	
GCR	126.74	137.29	138.28	-156.67	An endothermic peak
GCR: PEG-3350	125.96	137.09	138.01	-149.37	A shift in peak to left due to interaction between GCR and PEG-3350
GCR: PEG-4000	123.05	131.11	135.14	-159.46	A shift in peak to left due to interaction between GCR and PEG-4000
GCR: PEG-6000	125.85	135.61	137.81	-148.91	A shift in peak to left due to interaction between GCR and PEG-6000
GCR: PEG-8000	124.95	135.09	137.99	-150.05	A shift in peak to left due to interaction between GCR and PEG-8000
GCR: PEG-20000	190.32	131.22	135.60	-152.08	A shift in peak to left due to interaction between GCR and PEG-20000

GCR- Ganciclovir; PEG-Poly Ethylene Glycol

The thermogram of GCR was characterized by single sharp endotherm at 137.29ºC (indicates its melting). The DSC thermogram of the drug was observed to be in contract with the specifications.

GCR-PEG bases thermograms were also produced single endothermic peaks at 137.09ºC, 131.11ºC, 135.61ºC, 135.09ºC and 131.22ºC for GCR when combined (by microwave induced fusion) with PEG-3350, PEG-4000, PEG-6000, PEG-8000 and PEG-20000 respectively. These thermograms indicated that a little shift towards left when combined with PEG carriers may be due to the dissolution of GCR/mixing/its conversion into amorphous form. These thermograms indicate no sign of drug- excipients incompatibility of GCR with PEG carriers used.

The DSC thermo grams of GCR with PVP carrier

The DSC thermo grams of GCR with PVP carrier used was shown in tabulated in table 6.

Table 6: Endothermic events, Enthalpy and Inference of DSC data of EPVP

DSC	**Endothermic events (°C)**			**ΔH**	
Fusion Inference Sample	**T onset**	**T peak**	**Tend**	**Enthalpy (J)**	
GCR	126.74	137.29	138.28	-156.67	An endothermic peak
GCR: PVP K-12	125.96	136.52	138.95	-150.49	A shift in peak to left due to interaction between GCR and PVP K-12
GCR: PVP K-17	120.05	130.09	134.71	-157.51	A shift in peak to left due to interaction between GCR and PVP K-17
GCR: PVP K-25	126.17	134.33	137.02	-148.66	A shift in peak to left due to interaction between GCR and PVP K-25
GCR: PVP K-30	124.95	134.88	137.04	-151.44	A shift in peak to left due to interaction between GCR and PVP K-30
GCR: PVP K-90	123.15	133.82	135.11	-151.52	A shift in peak to left due to interaction between GCR and PVP K-90

GCR- Ganciclovir; PVP-Poly Vinyl Pyrrolidone

GCR-PVP bases thermograms were also produced single endothermic peaks at 136.52^{o}C, 130.09^{o}C, 134.33^{o}C, 134.88^{o}C and 133.82^{o}C for GCR when combined (by microwave induced fusion) with PVP K-12, PVP K-17, PVP K-25, PVP K-30 and PVP K-90 respectively. These thermograms indicated that a little shift towards the lower temperature when combined with PVP carriers, this may be due to the dissolution of GCR/mixing/its conversion into amorphous form. These thermograms indicate no sign of drug-excipients incompatibility of GCR with PVP carriers used.

The DSC thermograms of GCR with Poloxamer carrier

The DSC thermograms of GCR with Poloxamer carrier used was shown in tabulated in table 7.

Table 7: Endothermic events, Enthalpy and Inference of DSC data of EP

	Endothermic events		**(°C)**	**ΔH Fusion**	
DSC sample	**T onset**	**T peak**	**Tend**	**Enthalpy (J)**	**Inference**
GCR	126.74	137.29	138.28	-156.67	An endothermic peak
GCR:P108	120.86	129.30	134.12	-146.22	A shift in peak to left due to interaction between GCR and Poloxamer P-108
GCR:P188	121.06	125.19	131.65	-135.16	A shift in peak to left due to interaction between GCR and Poloxamer P-188
GCR:P237	119.98	128.01	133.26	-146.28	A shift in peak to left due to interaction between GCR and Poloxamer P-237
GCR:P338	120.23	129.62	134.15	-152.79	A shift in peak to left due to interaction between GCR and Poloxamer P-338
GCR:P407	122.99	133.75	134.16	-151.29	A shift in peak to left due to interaction between GCR and Poloxamer P-407

GCR- Ganciclovir; P-Poloxamer

GCR-Poloxamer bases thermograms were also produced single endothermic peaks at 129.30^{o}C, 125.19^{o}C, 128.01^{o}C, 129.62^{o}C and 133.75^{o}C for GCR when combined (by microwave melting) with Poloxamer-108, Poloxamer-188, Poloxamer- 237, Poloxamer-338 and Poloxamer-407 respectively. These thermograms indicated that a little shift towards the lower temperature when combined with Poloxamer carriers, because of the dissolution of GCR/mixing/its conversion into amorphous form. These thermograms indicate that there is no sign of drug-excipients incompatibility of GCR with Poloxamer carriers used.

The DSC thermograms of GCR with Urea carrier

The DSC thermograms of GCR with Urea carrier used was shown in tabulated in table 8.

Table 8: Endothermic events, Enthalpy and Inference of DSC data of EU

	Endothermic events		(°C)	ΔH Fusion	
DSC sample	**T onset**	**T peak**	**Tend**	**Enthalpy (J)**	**Inference**
GCR	126.74	137.29	138.28	-156.67	An endothermic peak
GCR: U	125.69	136.98	137.29	-151.39	A shift in peak to left due to interaction between GCR and Urea

GCR- Ganciclovir; U-Urea

GCR-Urea bases thermograms were also produced single endothermic peaks at 136.98ºC for GCR when combined (by microwave melting) with Urea. These thermograms indicated that a little shift towards the lower temperature when combined with Poloxamer carriers, because the dissolution of GCR/mixing/its conversion into amorphous form. These thermograms indicate that there is no sign of drug-excipients incompatibility of GCR with Urea.

Fourier Transform Infra-Red spectral analysis:
The FTIR spectra of Ganciclovir with carrier used was shown in figure 2 to 6.

The FTIR spectra of Ganciclovir with carrier used was shown in figure 2 to 6.

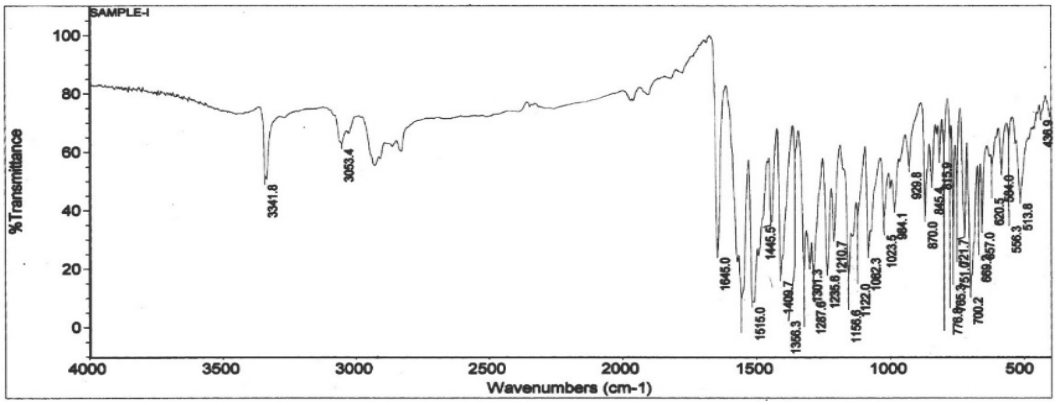

Fig. No. 2: FTIR spectrum of Ganciclovir pure drug

The FTIR spectra of Ganciclovir (alone) showed characteristic peaks at 1515.0 cm^{-1}(C- N stretching vibration); 1445.5 cm^{-1}, 1356.3 cm^{-1}, 1156.6 cm^{-1} and 1082.3 cm^{-1} (S=0 stretching vibrations); and 845.4 cm^{-1}, 776.8 cm^{-1} and 657.0 cm^{-1} (C-Cl stretching vibration), respectively.

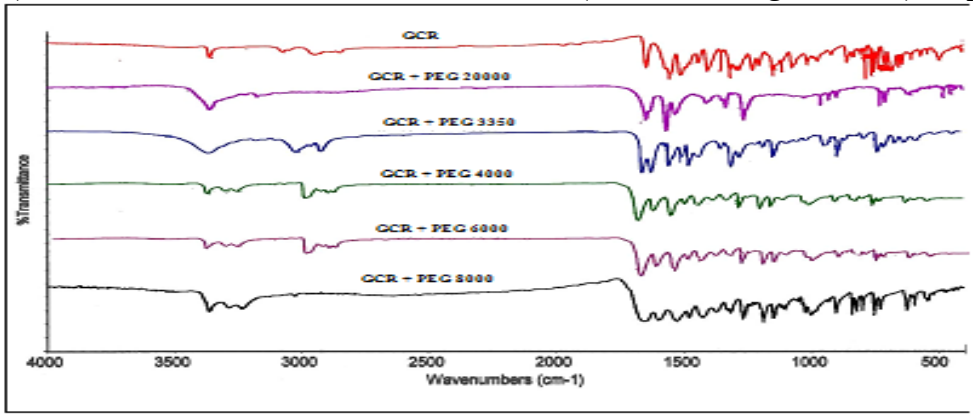

Fig. No. 3: FTIR spectrum of Ganciclovir with PEG

The spectra of blend corresponding to the GCR revealed that no negative chemical interaction of GCR with PEG bases used i.e., PEG- 3350, PEG-4000, PEG-6000, PEG-8000 and PEG-20000 (in solid dispersions).

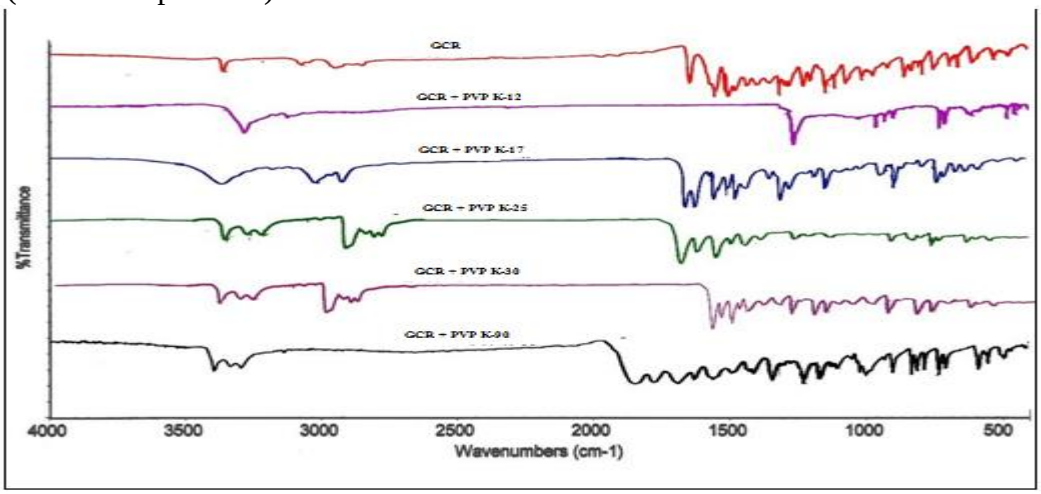

Fig. No. 4: FTIR spectrum of Ganciclovir with PVP

The spectra of blend corresponding to the GCR revealed that no negative chemical interaction of GCR with PVP carriers (PVP K-12, PVP K-17, PVP K-25, PVP K-30 and PVP K-90).

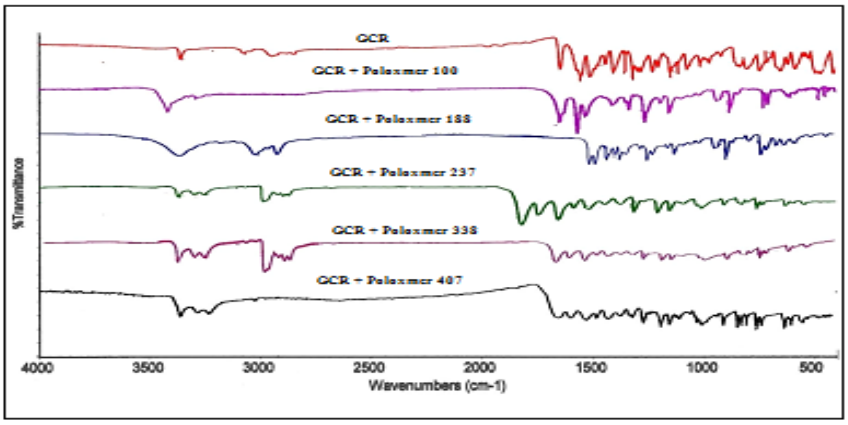

Fig. No. 5: FTIR spectrum of Ganciclovir with Poloxamer

The spectra of blend and the GCR revealed that no negative chemical interaction of GCR with Poloxamer carriers (P-108, P-188, P-237, P-338 and P-407).

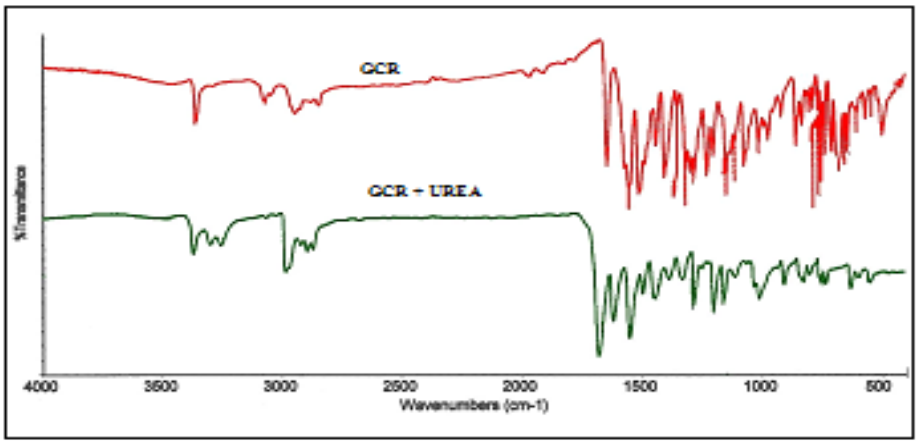

Fig. No. 6: FTIR spectrum of Ganciclovir with Urea

The spectra of blend and GCR revealed that no negative chemical interaction of GCR with Urea. The overall FTIR spectral study revealed that no negative chemical interaction of GCR with SDs carriers used (PEG, PVP, Poloxamer and Urea).

Thus, it can be concluded from the above-mentioned observations that though the drug molecules are hydrogen bonded with the polymers to some extent through sulphonamide groups, the overall symmetry of the drug molecule was not significantly affected.

Flow properties (Pre Compression)

The prepared GCR SDs when checked for flow characteristics which were represented in table 9 to

Table 9: Flow character specifications (Ganciclovir+ PEG)

Flow properties

Formulation	Angle of repose (^{0})	Bulk Density	Tapped Density	Carr's Index	Hausner Ratio
EPEG3-1	25.21±0.04	0.401±0.02	0.450±0.02	10.889±0.01	1.122±0.06
EPEG3-2	29.33±0.05	0.400±0.03	0.416±0.02	3.846±0.02	1.040±0.02
EPEG3-3	34.21±0.04	0.377±0.01	0.403±0.02	6.451±0.05	1.068±0.07
EPEG3-4	25.21±0.02	0.393±0.02	0.422±0.03	6.872±0.09	1.073±0.06
EPEG4-1	26.33±0.01	0.412±0.03	0.445±0.02	7.415±0.04	1.080±0.02
EPEG4-2	28.45±0.08	0.402±0.02	0.462±0.03	12.987±0.08	1.149±0.06
EPEG4-3	29.21±0.09	0.502±0.01	0.526±0.02	4.562±0.03	1.047±0.02
EPEG4-4	29.04±0.06	0.195±0.05	0.203±0.02	3.940±0.02	1.041±0.03
EPEG6-1	30.25±0.04	0.252±0.02	0.269±0.01	6.319±0.05	1.067±0.06
EPEG6-2	29.21±0.01	0.393±0.08	0.425±0.03	7.529±0.03	1.081±0.02
EPEG6-3	27.25±0.03	0.323±0.02	0.352±0.02	8.238±0.07	1.089±0.05
EPEG6-4	25.09±0.02	0.512±0.04	0.548±0.05	6.569±0.03	1.070±0.02
EPEG8-1	27.27±0.05	0.623±0.02	0.666±0.02	6.456±0.05	1.069±0.06
EPEG8-2	26.21±0.04	0.854±0.05	0.898±0.03	4.899±0.03	1.051±0.04
EPEG8-3	26.37±0.09	0.269±0.01	0.279±0.01	3.584±0.02	1.037±0.06
EPEG8-4	31.21±0.04	0.562±0.03	0.587±0.06	4.258±0.01	1.044±0.06
EPEG20-1	30.54±0.06	0.348±0.02	0.358±0.02	2.793±0.08	1.028±0.05
EPEG20-2	28.45±0.02	0.365±0.02	0.375±0.04	2.666±0.09	1.027±0.06
EPEG20-3	29.35±0.04	0.848±0.03	0.878±0.01	3.416±0.03	1.035±0.08
EPEG20-4	27.97±0.05	0.458±0.01	0.512±0.03	10.546±0.02	1.117±0.02

Values in mean ±SD; trials made (n=3)

Table 10: Flow character specifications (Ganciclovir+ PVP)

Flow properties

Formulation	Angle of repose (^{0})	Bulk Density	Tapped Density	Carr's Index	Hausner Ratio
EPVP12-1	28.37±0.09	0.135±0.02	0.144±0.01	6.250±0.03	1.066±0.03
EPVP12-2	30.20±0.12	0.369±0.01	0.399±0.03	7.518±0.02	1.081±0.05
EPVP12-3	31.52±0.06	0.659±0.03	0.677±0.03	2.658±0.07	1.027±0.02
EPVP12-4	29.43±0.07	0.658±0.01	0.691±0.04	4.775±0.02	1.050±0.03
EPVP17-1	26.38±0.04	0.941±0.03	0.985±0.07	4.467±0.08	1.046±0.08
EPVP17-2	27.96±0.15	0.286±0.01	0.303±0.03	5.610±0.04	1.059±0.01
EPVP17-3	28.34±0.06	0.385±0.02	0.432±0.02	10.876±0.02	1.122±0.03
EPVP17-4	32.26±0.10	0.365±0.01	0.401±0.03	8.977±0.09	1.098±0.04
EPVP25-1	33.50±0.06	0.285±0.01	0.298±0.01	4.362±0.03	1.045±0.03
EPVP25-2	29.15±0.08	0.654±0.03	0.668±0.04	2.095±0.01	1.021±0.02
EPVP25-3	29.30±0.04	0.256±0.01	0.287±0.01	10.801±0.07	1.121±0.03
EPVP25-4	28.05±0.06	0.748±0.02	0.795±0.02	5.911±0.045	1.062±0.03
EPVP30-1	26.37±0.09	0.458±0.01	0.521±0.03	12.092±0.02	1.137±0.01
EPVP30-2	31.24±0.06	0.136±0.02	0.142±0.01	4.225±0.03	1.044±0.09
EPVP30-3	30.56±0.08	0.195±0.03	0.213±0.06	8.450±0.02	1.092±0.04
EPVP30-4	29.49±0.06	0.358±0.02	0.385±0.03	7.012±0.02	1.075±0.03
EPVP90-1	29.37±0.08	0.365±0.01	0.407±0.02	10.319±0.05	1.115±0.03
EPVP90-2	28.95±0.06	0.458±0.02	0.489±0.03	6.339±0.02	1.067±0.08
EPVP90-3	29.36±0.07	0.526±0.04	0.536±0.03	1.865±0.01	1.019±0.01
EPVP90-4	32.65±0.05	0.956±0.07	0.978±0.03	2.249±0.02	1.023±0.03

Table 11: Flow character specifications (Ganciclovir+ Poloxamer)

Flow properties

Formulation	Angle of repose (^{0})	Bulk Density	Tapped Density	Carr's Index	Hausner Ratio
EP108-1	30.50±0.06	0.235±0.01	0.255±0.03	7.843±0.06	1.085±0.01
EP108-2	28.77±0.04	0.456±0.03	0.468±0.03	2.564±0.01	1.026±0.02
EP108-3	25.71±0.06	0.856±0.05	0.879±0.01	2.616±0.03	1.027±0.09
EP108-4	29.48±0.05	0.759±0.02	0.779±0.02	2.567±0.06	1.026±0.03
EP188-1	26.39±0.02	0.958±0.01	0.977±0.01	1.944±0.01	1.019±0.03
EP188-2	33.36±0.06	0.658±0.04	0.689±0.01	4.499±0.02	1.047±0.05

EP188-3	30.11±0.11	0.842±0.05	0.874±0.02	3.661±0.03	1.038±0.01
EP188-4	28.52±0.13	0.758±0.03	0.769±0.06	1.430±0.01	1.014±0.08
EP237-1	29.33±0.08	0.526±0.02	0.536±0.04	1.866±0.03	1.019±0.03
EP237-2	33.45±0.09	0.365±0.09	0.384±0.02	4.947±0.04	1.052±0.02
EP237-3	29.48±0.03	0.445±0.03	0.457±0.01	2.583±0.03	1.026±0.01
EP237-4	26.32±0.02	0.521±0.04	0.530±0.04	1.698±0.01	1.017±0.03
EP338-1	27.09±0.06	0.656±0.03	0.666±0.03	1.501±0.05	1.015±0.02
EP338-2	26.37±0.14	0.625±0.05	0.643±0.03	2.799±0.03	1.028±0.03
EP338-3	33.23±0.01	0.635±0.03	0.701±0.03	9.415±0.01	1.104±0.03
EP338-4	30.55±0.08	0.528±0.01	0.584±0.01	9.589±0.07	1.106±0.01
EP407-1	29.42±0.02	0.659±0.03	0.695±0.03	5.179±0.04	1.055±0.02
EP407-2	32.37±0.08	0.458±0.02	0.487±0.01	5.955±0.01	1.063±0.02
EP407-3	30.58±0.09	0.689±0.03	0.712±0.03	3.230±0.03	1.033±0.06
EP407-4	25.99±0.03	0.758±0.03	0.789±0.02	3.929±0.01	1.041±0.03

Values in mean ±SD; trials made (n=3)

Table 12: Flow character specifications (Ganciclovir+ Urea)

Flow properties

Formulation	**Angle of repose (^{0})**	**Bulk Densit**	**Tapped Density**	**Carr's Index**	**Hausner Ratio**
EU-1	29.52±0.03	0.584±0.08	0.597±0.03	2.177±0.03	1.022±0.01
EU-2	26.16±0.08	0.295±0.03	0.325±0.02	9.230±0.05	1.102±0.06
EU-3	29.84±0.02	0.359±0.02	0.398±0.01	9.799±0.08	1.109±0.02
EU-4	29.65±0.09	0.985±0.07	1.020±0.02	3.431±0.04	1.035±0.01

Values in mean ±SD; trials made (n=3)

Micromeritic properties (viz., the angle of repose, bulk density, tapped density, Carr's index and Hausner ratio) of prepared SDs (GCR SDs with PEG, PVP, Poloxamer and Urea bases) were evaluated before compression. The results of the angle of repose were found to be 25-30^o designates excellent flow characteristics. The compressibility index values were found up to 15%, this indicates in good to excellent flow properties. Additionally, the dispersions showed a Hausner ratio less than 1.25 is an indication of good flow ability.

CONCLUSION

The main theme behind this research work was to prepare GCR SDs using PEG bases (PEG3350, PEG 4000, PEG 6000, PEG 8000 and PEG 20000), PVP bases (PVP K-12, PVP K-17, PVP K-25, PVP K-30 and PVP K-90), Poloxamers (Poloxamer 108, Poloxamer 188, Poloxamer 237, Poloxamer 338, Poloxamer 407) and Urea.

REFERENCES

1. Nyol S, Gupta MM. Immediate drug release dosage form: a review. J Drug Delivery Thera. 3(2) (2013) 155-161.
2. Gordon L Amidon, Hans Lennernas, Vinod P Shah and John R Crison. A theoretical basis for a biopharmaceutics drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 12(3) (1995) 413-420.
3. Patel V, Patel K. Review on Immediate release dosage system. Int J Pharma Res Bio Sci. 1(5) (2012) 37-66.
4. Corrigan OE. Mechanism of dissolution of fast release solid dispersion. Drug Dev Ind Pharm. 1 (1985) 697 – 724.
5. Chatap VK, Gupta RD, Jaiswal NR. Recent advances immediate release technology. Asian Journal of Pharmaceutics. 1(4) (2007) 191-195.
6. Jain NK, Sharma SN. A textbook of professional pharmacy, 4th, Vallabh Prakashan, New Delhi, India, 2001.
7. Sofia AP, Dimitrios B, Konstantinos. A Microwave-Induced Enhancement of the Dissolution Rate of Poorly Water-Soluble Tibolone from Poly (ethylene glycol) Solid Dispersions. Journal of Applied Polymer Science. 108 (2008) 1249–1258.
8. Mourya D, Belamwar V, Tekade A. Microwave induced solubility enhancement of poorly water soluble atorvastatin calcium. 62 (11) (2010) 1599-606.
9. IKyrikou, SK Hadjikakou, DKovala Demertzi, K Viras, T Mavromoustakos. Effects of non-steroidal anti-inflammatory drugs in membrane bilayers. Chem. Phys. Lipids. 132 (2004) 157 – 169.
10. MB Boggara, R Krishnamoorti. Partitioning of non steroidal anti-inflammatory drugs in lipid membranes: a molecular dynamics simulation study. Biophys J. 98 (2010) 586 – 595.
11. Shipra S, Amrita M, Anurag V, Ashoke KG, Arun KM. A simple Ultraviolet spectrophotometric method for the determination of etoricoxib in dosage formulations. J Adv Pharm Technol Res. 3(4) (2012) 237–240.
12. Huang YT, Tsai TR, Cheng CJ, Cham TM, Lai TF, Chuo WH. Formulation design of an HPMC-based sustained tablet for pyridostigmine bromide as a highly hygroscopic model drug and its in vivo/in vitro dissolution properties. Drug DevInd Pharm. 33 (2007) 1183–91.
13. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Philadelphia PA Lea and Febiger (1987) 317-318.
14. Aulton ME. Pharmaceutics-The Science of Dosage Forms Design. 2nd ed. London Churchill Livingstone. (1988) 600.
15. Martin A. Physical Pharmacy. 4th ed. Maryland, USA: Lippincott Williams and Wilkins, (1991) 423.