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Development and evaluation of a mucoadhesive microsphere solid dispersion containing cefpodoxime

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Abstract:
Poorly water-soluble drug Cefpodoxime Proxetil is produced using solid dispersion, which enhances solubility and dissolution. The major goal of this study was to use the solvent evaporation technique to generate a solid dispersion of Cefpodoxime Proxetil in order to increase its solubility and speed of dissolution. The solid dispersions of Cefpodoxime Proxetil were made using water-soluble carriers such as Mannitol, Cyclodextrin, PEG-4000, and PEG-6000. F10 (1;1) has the best solid dispersion release profile with -cyclodextrin after examination. These microspheres have a 10% CAP enteric coating. The ideal MS2 formulation was chosen after thoroughly evaluating the aspects of the medication release. The solid dispersion, physical mixture dissolving rate, and characteristics of the drug were all discovered to be greater than those of the intact drug. No chemical incompatibility between the carriers and the medication was found in the FT-IR spectra.

Keywords: Mucoadhesive microspheres, Cefpodoxime Proxetil, Solid dispersions, Chemical Incompatibility

Introduction:

Cefpodoxime proxetil is an oral 3rd generation cephalosporin with a broad spectrum of antibacterial activity [1]. Solid dispersion is defined as a dispersion which is a drugs eutectic mixtures with water soluble carriers by melt of their physical mixtures. It help in the solubility enhancement. so here main focus is to improve cefpodoxime proxetil dissolution rate by preparing solid dispersion. Different water soluble polymer is used like manitol,β-CYCLODEXTRIN, PEG 4000, PEG 6000.[2]

The release profile of drug formulation using solid dispersions achieved by the carrier manipulation. Parameters, such as, composition, drug crystallinity, carrier molecular weight particle wettability and porosity that successfully controlled is produce improvements in

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bioavailability. [2] solid dispersion is having lots of advantage like improvement in drug porosity,masking of taste , colour , reduction in particle size.[2,3]

Applications 1. To enhance the drug absorption 2. To obtain a homogeneous a small amount distribution of drug in solid state; [4]

TYPES OF SOLID DISPERSION[5]

Eutectic mixtures**,** Discontinuous solid solutions, Glass solution and suspensions **Amorphous** precipitation in crystalline matrix**,** Subsitutional solid dispersions**,** Solid solution

METHODS OF PREPARATION OF SOLID DISPERSIONS [5-7]

The solid dispersion systems are prepared by following method,

Melting method

Melting (fusion) method was to the accurately weighed amount of PEG-4000, and PEG-6000 melted in a porcelain dish at 80-85°C and calculated amount of cefpodoxime proxetil and mixing for 1-2 min followed quick cooling than kept in a dessicator under vacuum for 24 hrs.

Solvent method:

The drug and excipients are dissolved in require volume of methanol with vigorous stirring. When the solvent was completely evaporated at 40-45°C with continuous stiring and to obtained by a dry granule. Solid dispersion was stored in a air tight container and then further use. `

Mucoadhesive Microspheres

This system is remained in close contact with mucous membrane, absorption tissue, drug release at action site leading to bioavailability increase both local and systemic effects. Oral route of drug administration is constituting most convenient and drug delivery system preferred to systemic circulation of body.

The success of microspheres is limited due to short residence time at absorption. Therefore, advantage has providing intimate contact of drug delivery system with absorbing membrane. Microspheres mucoadhesion or bioadhesion is defined as a form of two materials in which at least one is biological in nature for a long time period by interfacial forces So there are various **Advantages of mucoadhesive microspheres drug delivery system like** improving API bioavailability, tissue targeting, increased residence time etc.. [6]

DRUG PROFILE

Structure

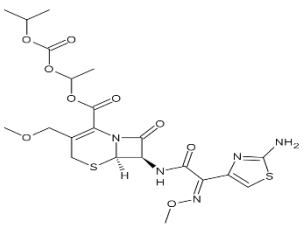

Figure 1:- Structure of cefpodoxime proxetil

Physical and chemical properties

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IUPAC name :- (6,7)-7-{[(2)-2-(2-amino-1,3-thiazol-4-yl)-2-methoxyimino-acetyl]amino}-3-(methoxy methyl)-8-oxo-5-thia-1-azabicyclo[4]oct-2-ene-2-carboxylic acid.[1]
Empirical formula = $C_{15}H_{17}N_5O_9S_2$
Molecular weight = 427.458 g/mol
Melting point = 148.5° C
Category = antibiotic

Objective of the Study

1. To formulate solid dispersion of cefpodoxime proxetil and then incorporate them into mucoadhesive microspheres.
2. To formulate solid dispersion of the drug and its effect on the solubility of the drug.
3. To formulate mucoadhesive microspheres for the sustained release of the drug.
3. To evaluate the prepared formulation for following parameters like Drug content uniformity, Encapsulation efficiency, In-vitro release study,*Ex-vivo* mucoadhesive property of the microspheres, Stability study

REAGENTS USED:

Table-1:- List of Reagents used

S.NO.	REAGENTS USED
1.	Ethanol
2.	Dichloromethane
3.	Hydrochloric acid
4.	Distilled water
5.	Methanol
6.	Ether
7.	Sodium hydroxide
8.	Potessium dihydrophosphate
9.	N-Octane

All Chemicals Used In Experiment Were Analytical Grade and Purchased From Their Respective Commercial Sources

EQUIPMENTS USED

Table- 2:- List of Equipments used

S.NO	INSTRUMENTS
1	Electronic Weighing Balance
2	UV-Vis Spectrophotometer

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3	Dissolution test apparatus
4	Hot Air Oven
5	Heating mantle
6	Magnetic Stirrer
7	Stability Chamber

METHODOLOGY

Preformulation studies:

IDENTIFICATION OF DRUG

Identification of drug was performed by following technique.

Physical Evaluation: The drug was evaluated for its physical form and organoleptic properties.

wavelength maximum (ʎmax) of cefpodoxime proxetil

The cefpodoxime proxetil solution of (6 µg/ml) was prepared in water, methanol, phosphate buffer 6.8, phosphate buffer 7.8 and then scanned using shimadzu, double beam uv-vis spectrophotometry 1700). the scanning range was between 200nm to 400nm.

Ultra violet spectroscopy: the cefpodoxime proxetil was weighed accurately 100mg and dissolved in distilled water or other solvent. the solution volume was made up 100 ml. the solution was marked as stock solution-i and 10ml of stock solution was taken and solution volume was made up 100ml.(stock-ii).

1). from stock-ii, dilution having concentration 5µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml and 25 µg/ml were prepared.

2). above the prepared solution were observed in double beam uv-spectrophotometer (shimadzu) to measure absorbance, increasing order of concentration.

IR spectroscopy:

1mg of the sample and 300mg of kbr were taken in morter and triturated. a small amount of triturated sample was taken into a pellet maker and compressed at 10kg/cm2. the pellet was kept in sample holder and scanned from 4000cm-1 to 400cm-1. the drug´s infrared spectrum sample was obtained by using ftir-8400s.

Melting point:

Melting point of drug was determined through taking small amount of drug in a capillary tube closed from one end and was to placed in melting point apparatus and temperature at which drug melt was noted. [16,17]

Partition coefficient:

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The partition coefficient study was performed by using n-octanol as oil phase and water as aqueous phase. cefpodoxime proxetil were taken in a separating funnel. the mixture was shaken continuously for 30 min until equilibrium was reached and stands for overnight. the two phases were separate within themselves. then the both phase were analyzed for respective drug content measuring absorbance by uv spectrophotometer at 235nm.

Method: 50 mg of drug was dissolved in 25 ml of octanol mixed with 25ml of phosphate buffer (ph 7.4) the solution was taken in a separating funnel and shaken for 30 min and allow to stand for until complete separation was achived. 1 ml of aqueous layer was transferred in to the 10 ml of volumetric flask and make up the volume with water. the absorbance of solution was 235 nm.

Solubility studies

The solubility of cefpodoxime proxetil was study in the various aqueous and non-aqueous solvent. the solubility was determined by exposing as excess of drug powder to the solvent and the assaying after equilibrium has been established. excess amount of cefpodoxime proxetil was added to different solvent and then kept for 24 hrs at a room temperature. 8

Drug polymer interaction study

The drug-polymer compatibility studies were designed to ensure the stability to final formulation and physical studies were designed to ensure the stability of final formulation. the drug´s physical mixture and excipients in ratio of 1:1 was placed in glass vials, sealed and store in 400ºc and 75% rh. the sample was withdrawn at a time of interval of 15 and 21 day and examined for physical and chemical integrity of a drug and excipients. the drug polymer compatibility was further confirmed that taking ir spectrum of drug, polymer and physical mixture of drug polymer in ratio 1:1. the ir spectrum of drug physical mixture and polymer was taking by placing them in stability chamber at a temperature of 400ºc and 75% rh for 21 days.

THE DRUG POLYMER RATIO

TABLE 3. DRUG-POLYMER RATIO

S.NO.	Material	Quantity (mg)
1	**CEFPODOXIME PROXETIL**	100mg
2	drug + peg-4000	100mg+ 100mg
3	drug + peg-6000	100mg+ 100mg
4	drug + manitol	100mg+ 100mg
5	drug +β-cyclodextrin	100mg+100mg

FORMULATION OF CEFPODOXIME PROXETIL SOLID DISPERSION

Solid dispersions are prepared by using the solvent evaporation method.

Solvent evaporation method

The drug and excipients are dissolved in require volume of methanol with stirring. As solvent was completely evaporated cefpodoxime proxetil´s solid dispersion was left behind and then kept in dessicator for removal. Prepared cefpodoxime proxetil´s solid dispersion was kept for further use. [9,10]

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Table no. 4:- Formulation of Solid dispersion

Ingredients formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg
PEG 4000	500 mg	1.0 gm	_	_	_	_	_	_	_	_	_	_
PEG 6000	_	_	500 mg	1.0 gm	_	_	_	_	_	_	_	_
Mannitol	_	_	_	_	250 mg	500 gm	1.0 gm	1.5 gm	_	_	_	_
β-cyclodextrin	_	_	_	_	_	_	_	_	250 mg	500 mg	1.0 gm	1.5 gm

Evaluation of cefpodoxime proxetil solid dispersion

Solubility

The cefpodoxime proxetil is insoluble in water and cefpodoxime proxetil is intrinsic soluble in pure water at room temperature and found to be 0.084mg/ml.

Percentage practical yield

Percentage practical yield was calculated to know about percent yield and it helps in selection of appropriate ratios of solid dispersion .Solid dispersions were collected and weighed to determine practical yield from the following equation-

$$\% \text{ yield} = \frac{\text{Practical mass} * 100}{\text{Theorical mass (Drug + Carrier)}}$$

Drug Content

Preparation equivalent 50 mg model drug. It was weighed and dissolved separately in methanol 50 ml. Solutions were diluted absorbance of solutions. It was determined at 262 nm by UV spectrophotometer.

$$\text{Drug content} = \frac{(\text{Final weight} - \text{initial weight}) * 100}{\text{Initial weight}}$$

In-vitro dissolution

In-vitro dissolution studies were done to compare dissolution rate of solid dispersions with pure drug cefpodoxime proxetil and physical mixtures. It was performed in USP paddle apparatus using 900ml pH 7.4 phosphate buffer solution and temperature 37±1ºC. [12-13]

FORMULATION OF CEFPODOXIME PROXETIL SOLID DISPERSION IN MUCOADHESIVE MICROSPHERE

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TABLE 5: THE COMPOSITION OF CEFPODOXIME PROXETIL SOLID DISPERSION IN MUCOADHESIVE MICROSPHERE

INGREDIENT	MS1	MS 2	MS_3	MS4
CEFPODOXIME PROXETIL solid dispersion*	1000 mg	1000 mg	1000 mg	1000 Mg
Calcium carbonate	10 %	10 %	10 %	10 %
Sodium alginate in 100 ml water	500 mg	1000 mg	1500 mg	2000 mg
CAP	10%	10%	10%	10%

***CEFPODOXIME PROXETIL SOLID DISPERSION CONTINING 1:1 DRUG AND BETA-CYCLODEXTRIN**

PROCEDURE FOR CEFPODOXIME PROXIETIL SOLID DISPERSION PREPARATION INCORPORATED IN MUCOADHESIVE MICROSPHERE [9,14,17]

measured the quantity of cefpodoxime proxetil solid dispersion were added in 100 ml solution of sodium alginate in a beaker and were stirred at high speed of using mecahnical stirrer and after 30 minute remove from mechanical stirrer and form a homogenous thick solution. the above solution was added dropwise using syringe (18cc) in beaker containing calcium carbonate solution (10%) and was continuously stirred for 4hrs at stirring speed of 1400rpm. after 4hrs filter and separate the microspheres and dried at 60oc in oven for 5 hrs . the microspheres were coated by cap using spray coating method .

EVALUATION OF CEFPODOXIME PROXIETIL SOLID DISPERSION INCORPORATED IN MUCOADHESIVE MICROSPHERE

Percent Practical Yield

Percentage practical yield were calculated to know about percent yield and help in selection of appropriate ratios of solid dispersion .Solid dispersions were collected and weighed to determine practical yield from the following equation[18,19]

$$\% \text{ yield} = \frac{\text{Practical mass} * 100}{\text{Theorical mass (Drug + Carrier)}}$$

Drug Content

Prepared 50 mg of model drug was weighed accurately that dissolved separately in 50 ml methanol and solutions were diluted. The absorbance of solutions was determined at 262 nm by UV spectrophotometer.

$$\text{Drug content} = \frac{(\text{Final weight} - \text{initial weight}) * 100}{\text{Initial weight}}$$

Entrapment Efficiency

25 mg of dried microsphere were weighted accurately and drug was extracted from microspheres
by digesting for 24 hrs with 10 ml of SGF (pH 6.8). During this period the suspension was agitated. After 24 hrs the suspension was centrifuged at 2000 rpm for about 3 minutes. The solution was filtered through 0.45 mm membrane filter, and the filtrate was analyzed for drug content at 263 nm[20].

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The percent encapsulation efficiency is calculated by following equation:-

$$\text{Percentase entrapment} = \frac{[\text{Final amount} - \text{initial amount}] * 100}{\text{Initial amount}}$$

Mucoadhesive test

Mucoadhesive property of microspheres prepared using by different methods is evaluated through in-vitro mucoadhesion test method called as wash-off method. The goat stomach mucosa is tied in glass slide by a thread. Microspheres are spread into wet rinsed tissue specimen and prepared slide is hung in grooves of USP tablet disintegrating test apparatus than switched on apparatus, up and down movements of tissue for 2 hrs in beaker of disintegration test apparatus that contained stimulated gastric fluid is pH 1.2. Microspheres remaining at surface of gastric mucosa are collected and percentage of remaining microspheres is calculated. The percentage mucoadhesion is calculated by using the following formula:

$$\text{Percent mucoadhesion} = \frac{\text{Weight of adhered microsphere} * 100}{\text{Weight of applied microspheres}}$$

In vitro Dissolution Studies

The USP dissolution apparatus (Type-II) was used for evaluation of release profile of mucoadhesive microsphere solid dispersions. Dissolution medium was containing 900 ml pH 6.8 phosphate buffer kept at 37 ± 0.1°C. The solid dispersion of mucoadhesive microsphere was taken in muslin cloth then kept in basket of dissolution apparatus and rotated at 100 rpm. The samples of 5ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 235 nm and withdrawn samples were replaced by fresh buffer solution. Each preparation values were calculated.[21,22]

Swelling index

Swelling index is used for sodium alginate microspheres characterization. Different solution (100 mL) are taken like distilled water, pH 1.2, 6.8, 7.4 buffer solution are taken. The alginate microspheres (100 mg) are placed in wire basket and kept on above solution. Swelling is allowed at 37ºC that changes weight variation between initial microspheres weight and final weight after swelling is measured weight by some interval.

Swelling index of microsphere is calculated by using formula:-

$$\text{Swelling index} = \frac{(\text{mass of swollen microspheres} - \text{mass of dry microspheres}) * 100}{\text{Mass of dried microspheres}}$$

Scanning Electron Microscopy (SEM)

The microspheres surface morphology is determined by SEM method. Microspheres are mounted directly on SEM sample with sticking tape and coated with gold film under decrease pressure in this method. The drugs Scanning Electron Photomicrographs loaded microspheres are taken a small amount of microspheres spread on gold stub. Afterwards stub containing sample is placed in Scanning electron microscopy (SEM).It is taken at acceleration 20 KV voltage and chamber pressure 0.6 mm Hg.[23]

Stability studies

Stability studies is evaluate by placing the microspheres in screw capped glass container and stored at following conditions:-

1. Ambient humid condition
2. Room temperature (27 +/- 2ºC)

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3. Oven temperature (40 +/- 2ºC)
4. Refrigerator (5ºC - 80ºC).

This is carried out of 60 days and drug content of microsphere is analyzed. [25,26]

RESULT AND DISCUSSION

Preformulation Studies

PHYSICAL EVALUATION: THE DRUG WAS EVALUATED FOR ITS PHYSICAL FORM AND ORGANOLEPTIC PROPERTIES.

ORGANOLEPTIC PROPERTIES AND PHYSICAL FORM OF CEFPODOXIME PROXETIL ARE FOLLOWING

TABLE NO.5:- ORGANOLEPTIC PROPERTIES AND PHYSICAL FORM OF CEFPODOXIME PROXETIL

S. NO.	ORGENOLEPTIC PROPERTIES	
1	DESCRIPTION	FINE CRYSTALLINE POWDER
2	COLOUR	YELLOWISH WHITE COLOUR
3	ODOUR	PUNGENT
4	TASTE	TASTELESS

WAVELENGTH MAXIMUM (ʎmax) OF CEFPODOXIME PROXETIL

The cefpodoxime proxetil solution of (6 µg/ml) was prepared in water, methanol, phosphate buffer 6.8, phosphate buffer 7.8 and then scanned using shimadzu, double beam uv-vis spectrophotometry 1700). the scanning range was between 200nm to 400nm maximum lemda max was obtained ʎmax 235 nm [24]

Solubility Study

Solubility Study of Drug in Different Solvents

TABLE NO.6:-Solubility Study of Drug in Different Solvents

S. No.	Solvents	Solubility	1gm drug in ml solvent
1	DCM	Freely soluble	7
2	Chloroform	Soluble	20
3	Methanol	Soluble	25
4	Ethanol	sparingly Soluble	65
5	Distilled Water	Insoluble	20,000

Partition coefficient

1. Partition coefficient of Drug in n-Octanol and water

Partition coefficient value ofdrug in n-octanol and water was found to be 1.34.

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2. Partition coefficient of Drug in Octanol and pH 6.8 phosphate buffer

Partition coefficient value of drug in phosphate buffer (pH6.8) was found to be 1.41.

3. Partition coefficient of Drug in Octanol and pH 7.4 phosphate buffer

Partition coefficient value of drug in Octanol and phosphate buffer (pH 7.4) was found to be 1.45.

8.1.5. Melting Point

Table-NO.7:- Melting point of cefpodoxime proxetil

S.No.	Melting point (°C)	Average ± S.D.
1	104.7	104.7 ± 0.5
2	105.3	
3	104.2	

The above experiment result revealed that observed melting point value i.e. 104.7°C of model API was matched with value given in standard literature. Hence it was used as preliminary identification tool.

QUANTITATIVE ESTIMATION OF DRUG

Praparation of celibration curve of cefpodoxime proxetil indefferent solvent

Preparation of calibration curve of cefpodoxime proxetil in methanol (λ_{max} 235 nm)

Table-NO.8- Calibration curve of cefpodoxime proxetil in methanol

S.NO	CONCENTRATION (µg/ml)	ABSORBANCE
1	5	0.304
2	10	0.381
3	15	0.45
4	20	0.483
5	25	0.547

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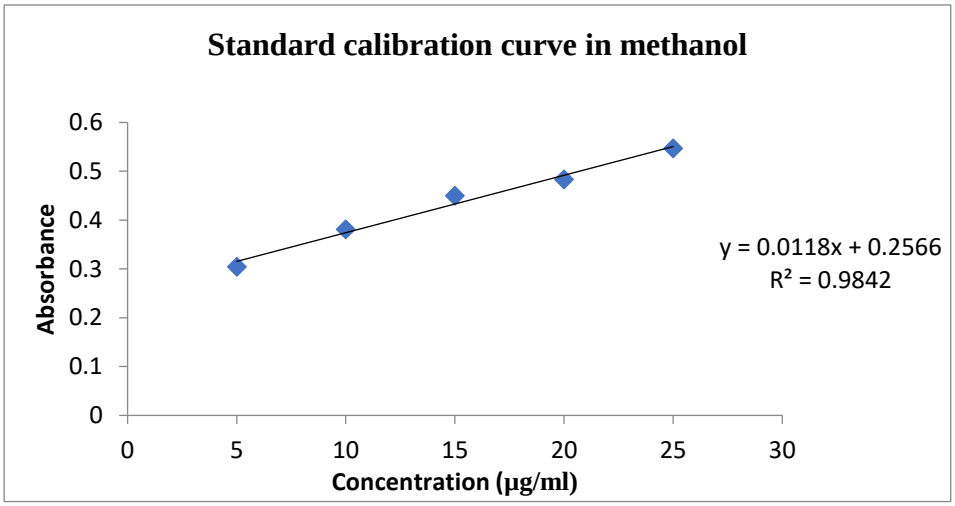

Figure-2:- Calibration curve of cefpodoxime proxetil in methanol

Preparation of cefpodoxime proxetil's calibration curve in phosphate buffer pH 6.8 (λ_{max} 235 nm)

Table-NO.9:- The cefpodoxime proxetil's calibration curve in phosphate buffer pH 6.8

S. No.	Concentration (µg/ml)	Absorbance
1	5	0.258
2	10	0.372
3	15	0.58
4	20	0.644
5	25	0.779

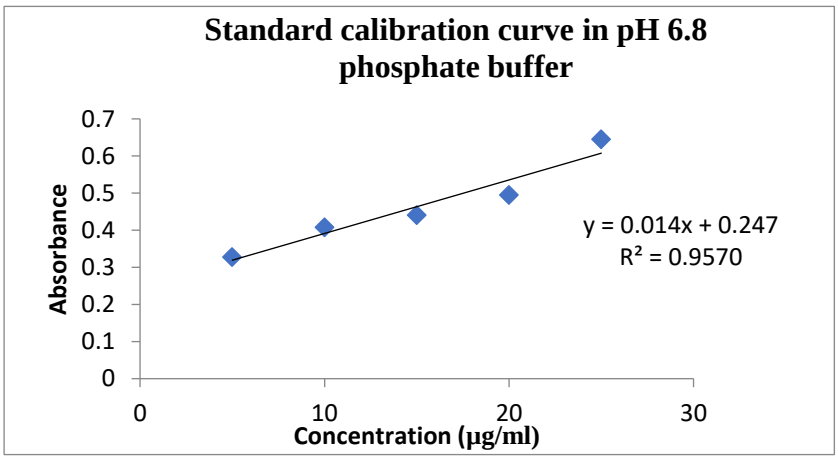

Figure-3:- Calibration curve of cefpodoxime proxetil in phosphate buffer pH 6.8

Preparation of cefpodoxime proxetil's calibration curve in 0.1N HCl (λ_{max} 235nm)

Table-NO.10- Calibration curve of cefpodoxime proxetil in 0.1N HCl

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S.NO.	Concentration (µg/ml)	Absorbance
1	2	0.016
2	4	0.029
3	6	0.041
4	8	0.052
5	10	0.068

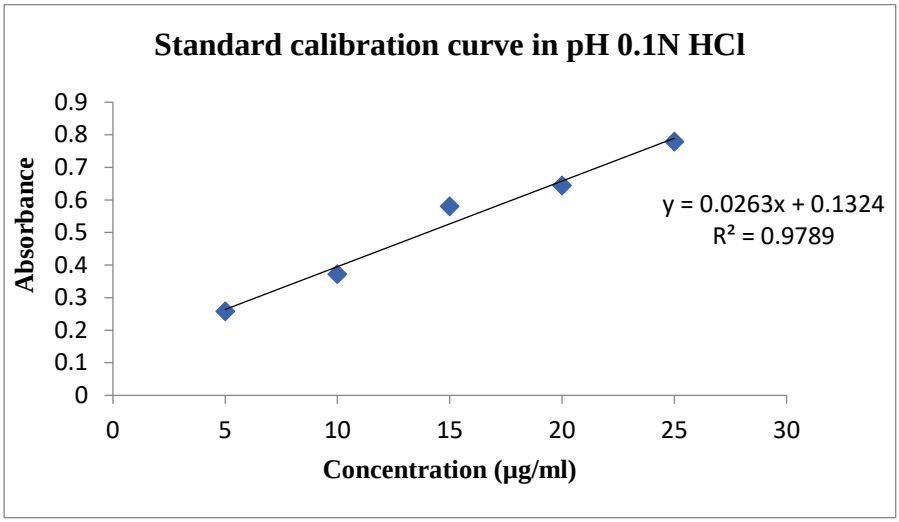

Figure-4:- Calibration curve of cefpodoxime proxetil in 0.1N HCl

D. Preparation of calibration curve of cefpodoxime proxetil in phosphate buffer pH- 7.4 (λ_{max} 235nm)

Table-NO.11:- Calibration curve of cefpodoxime proxetil in phosphate buffer pH-7.4

S.NO.	Concentration (µg/ml)	Absorbance
1	2	0.024
2	4	0.034
3	6	0.043
4	8	0.054
5	10	0.063

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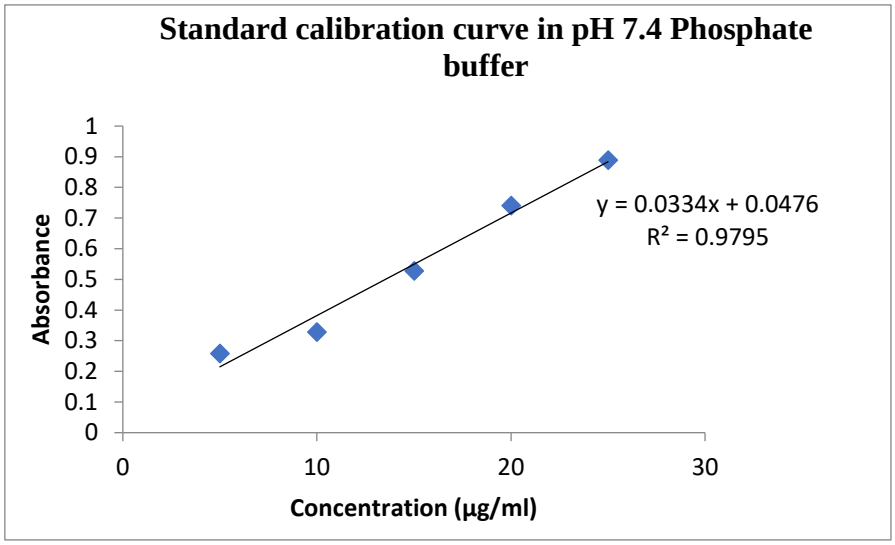

Figure-5

Calibration curve of cefpodoxime proxetil in phosphate buffer pH-7.4

As per the experimental result all four prepared standard curve having regression value above 0.95, which signify the reproducibility and linearity.

IR SPECTROSCOPY

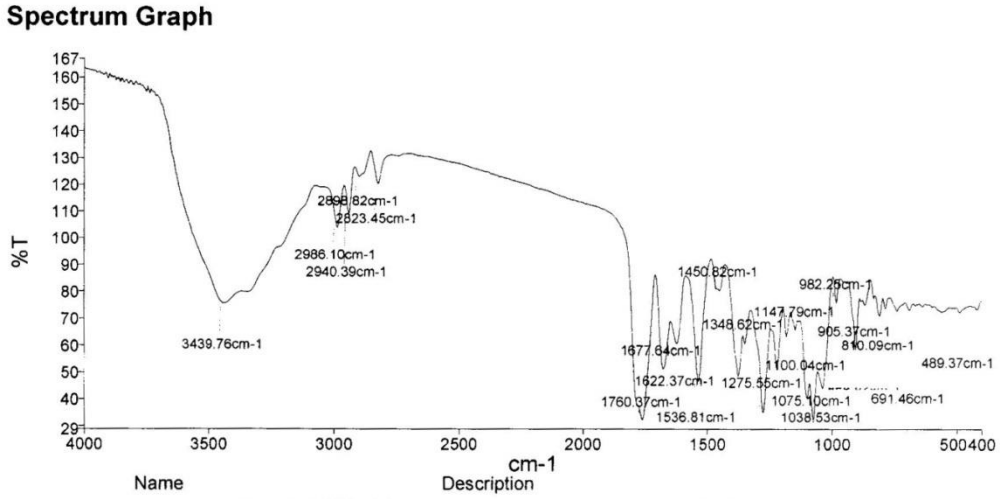

Figure-6:- FTIR of cefpodoxime proxetil

DRUG POLYMER INTERACTION STUDY

The drug and excipient were taken in 1:1 ratio mixed properly using a poly bag. Now the mixtures were transferred into the glass vials and samples were placed in stability chamber at 40^0C for 21 days.

Through Fourier Transform Infrared Spectroscopy:.

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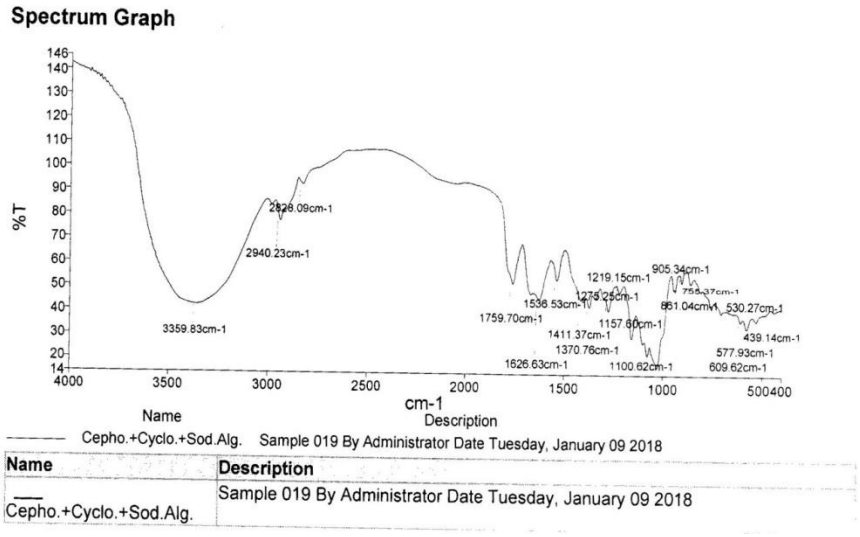

Figure-7:- FTIR of cefpodoxime proxetil with beta-cyclodextrin and sod. alginate polymer

Evaluation of solid dispersion

Percentase Practical yield

% practical yield of solid dispersion using defferent polymer

Table NO.12:- % practical yield of cefpodoxime proxetil solid dispersion using different polymer ratio

Formulation	% practical yield
F1	87
F2	79.1
F3	80.3
F4	72.4
F5	82.6
F6	85.6
F7	88.5
F8	79.7
F9	86.5
F10	90.7
F11	89.7
F12	83.4

The twelve formulations are prepared using different polymer ratio were evaluated. The percentase practical yield range for all the formulation were founded to be 79.1–90.7. The formulation F10 which contain1:1 drug polymer ratio showed higher % practical yield 90.7 %.

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Drug content

Drug content of cefpodoxime proxetil solid dispersion using differentpolymer ratio

Table NO.13:- Drug content of cefpodoxime proxetil solid dispersion using different polymer ratio

Formulation	Drug content
F1	86.6
F2	84.5
F3	78.7
F4	82.3
F5	74.8
F6	74.7
F7	75.3
F8	78.7
F9	77.7
F10	89.4
F11	87.2
F12	85.6

The twelve formulations are prepared using different polymer ratio were evaluated. The drug content range for all the formulation were founded to be 74.7-89.4. The formulation F10 which contain 1:1 drug polymer ratio showed higher drug content 89.4 %.

In-vitro dissolutionTable

In-vitro dissolution of solid dispersion using defferent polymer

Table NO. 14:- In-vitro dissolution of solid dispersion using PEG 4000 & 6000

Time (min)	Percentage drug relase of different ratio of PEG solid dispersion			
	Cefpodoximeproxetil + PEG- 4000		Cefpodoximeproxetil + PEG-6000	
	F_1 (1:1)	F_2 (1:2)	F_3 (1:1)	F_4 (1:2)
0	0	0	0	0

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10	27.5	28.2	11.8	10.45
15	38.9	41.3	26.75	16.75
30	41.5	53.4	36.9	24.7
45	56.7	64.4	40.1	32.9

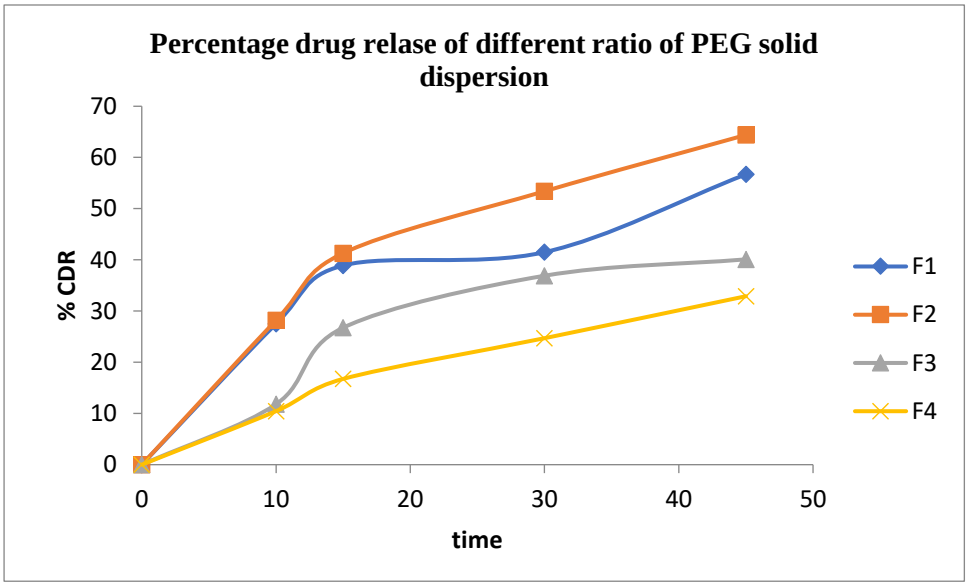

Figure-8:- Percentage drug relase of different ratio of PEG solid dispersion

The four formulations are prepared using different PEG 4000 & 6000 polymer ratio were evaluated. The formulation F2 which contain 1:1 drug polymer ratio showed higher % CDR as showed in fig. 8.

Table NO.15:- In-vitro dissolution of solid dispersion using mannitol

Time (min)	**Percentage drug relase of different ratio of solid dispersion**			
	Cefpodoxime proxetil + Mannitol			
	F_5 (1:0.5)	F_6 (1:1)	F_7 (1:1.5)	F_8 (1:2)
0	0	0	0	0
10	20.2	23.7	27.5	26.6
15	27.3	32.1	42.1	37.5
30	36.1	37.9	47.9	41.8
45	41.5	43.9	54.5	48.8

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Time (min)	Percentage drug relase of different ratio of solid dispersion			
	Cefpodoximeproxetil + β-Cyclodextrin			
	F_9 (1:0.5)	F_{10} (1:1)	F_{11} (1:1.5)	F_{12} (1:2)
0	0	0	0	0
10	57.5	53.2	55.8	50.4
15	68.9	61.3	67.5	60.7
30	71.5	74.4	73.9	67.7
45	73	89.4	80.1	71.2

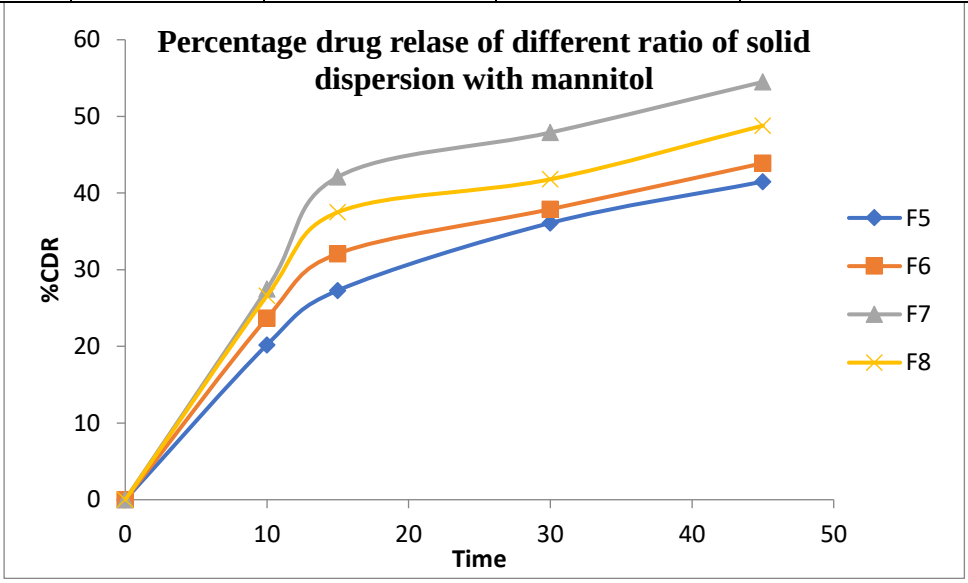

Figure no. 9:- Percentage drug relase of different ratio of mannitol solid dispersion

The four formulations are prepared using different mannitol ratio were evaluated. The formulation F7 which contain 1:1 drug polymer ratio showed higher % CDR as showed in fig. 9.

Table NO.16:- In-vitro dissolution of solid dispersion using β-Cyclodextrin

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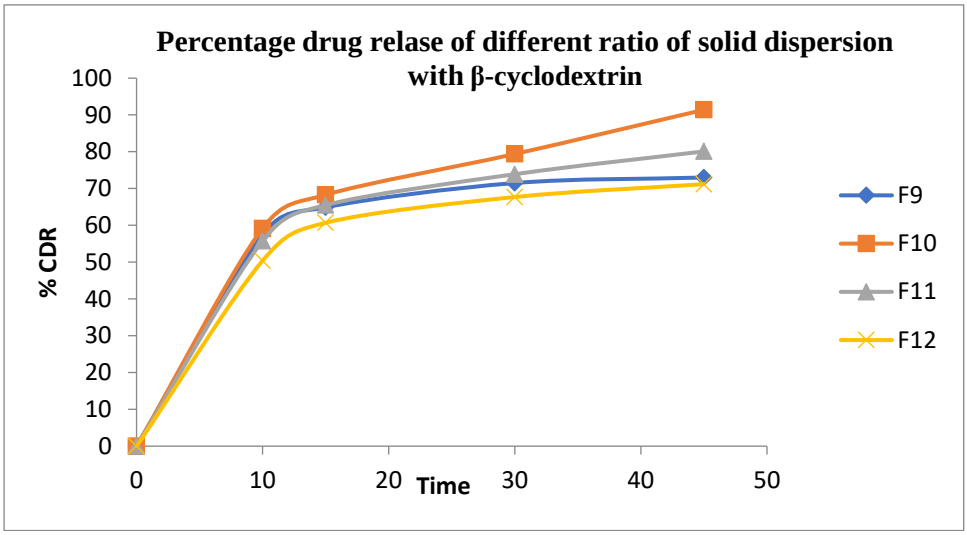

Figure no. 10:- Percentage drug relase of different ratio of β-Cyclodextrin solid dispersion

The four formulations are prepared using different β-Cyclodextrin ratio were evaluated. The formulation F10 which contain 1:1 drug polymer ratio showed higher % CDR as showed in fig. 10.

8.4. Comparative dissolution profile of cefpodoximeproxetil solid dispersion with different polymer and pure drug

Table NO.17:- Comparative dissolution profile of cefpodoximeproxetil solid dispersion with different polymer and pure drug

Time (min)	Percentage drug relase of different solid dispersion formulation and pure drug				
	Drug	F_2 (1:2)	F_3 (1:1)	F_7 (1:1.5)	F_{10} (1:1)
0	0	0	0	0	0
10	10.12	28.2	11.8	27.5	53.2
15	14.34	41.3	26.75	42.1	61.3
30	21.82	53.4	36.9	47.9	74.4
45	29.08	64.4	40.1	54.5	89.4

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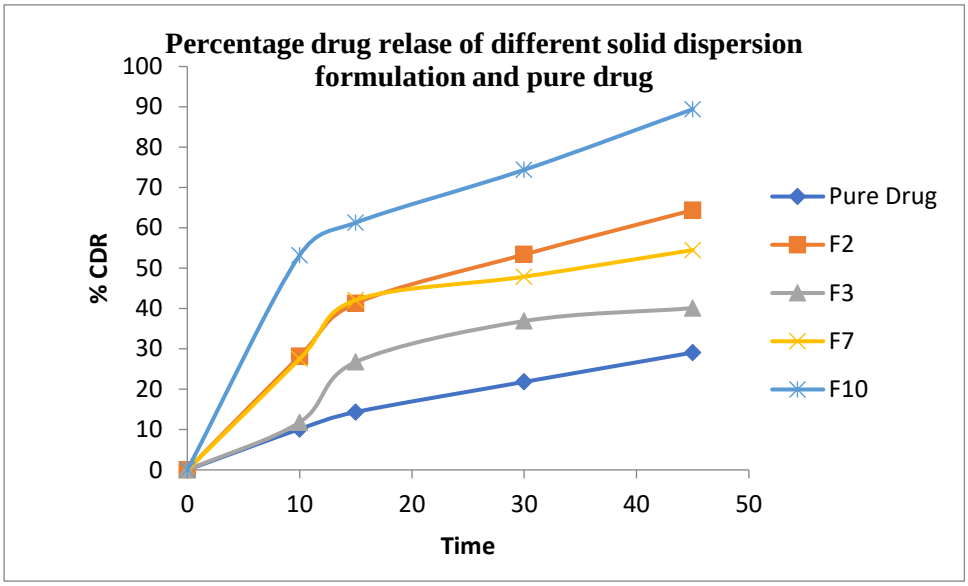

Figure no.-11:- Comparative dissolution profile of cefpodoximeproxetil solid dispersion with different polymer and pure drug

The five formulations are prepared using different polymer ratio and pure drug were evaluated. The formulation F10 which contain 1:1 drug polymer ratio showed higher % CDR as showed in fig. 11.

8.5. Evaluation of Microsphere

All the prepared mucoadhesive microspheres were evaluated by prelimanary steps such as visual apperance and drug content.[26]

8.5.1.% Practical yield

% practical yield of defferent ratio sodium alginate microsphere

Table NO.18:- % practical yield of defferent ratio of sodium alginate microsphere

Formulation	% practical yield
MS1	85.4
MS2	90.4
MS3	88.3
MS4	85.3

The four formulations are prepared using different sodium alginate ratio were evaluated. The percentase practical yield range for all the formulation were founded to be 85.3–90.4. The formulation MS2 which contain1:1 drug polymer ratio showed highest % practical yield 90.4 %. [30]

Drug content

Drug content of different ratio sodium alginate microsphere

Table NO.19-Drug content of different ratio sodium alginate microsphere

Formulation	Drug content

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MS1	74.3
MS2	86.3
MS3	83.5
MS4	79.0

The four formulations are prepared using different polymer ratio were evaluated. The drug content range for all the formulation were founded to be 74.3–86.3. The formulation MS2 which contain1:1 drug polymer ratio showed highst % practical yield 90.7 %.

8.5.3 Entrapment efficacy

Entrapment efficacy of different ratio sodium alginate microsphere

Table NO.20:-Entrapment efficacy of different ratio sodium alginate microsphere

Formulation	Entrapment efficacy
MS1	72.5
MS2	86.3
MS3	87.5
MS4	89.0

The four formulations are prepared using different polymer ratio were evaluated. The entrapment efficacy range for all the formulation were founded to be 72.5-89.0. The formulation MS4 which contain1:2 drug polymer ratio showed higher entrapment efficacy 89.0 %.

Mucoadhesive test

Mucoadhesive testofdefferent ratio sodium alginate microsphere

Table NO.21:- Mucoadhesive testofdefferent ratio sodium alginate microsphere

Formulation	Mucoadhesion
MS1	74.3
MS2	86.3
MS3	88.5
MS4	92.3

The four formulations are prepared using different polymer ratio were evaluated. The mucoadhesion for all the formulation were founded to be 73.5-92.3. The formulation MS4 which contain1:2 drug polymer ratio showed higher mucoadhesion 92.3 %. [27]

Swelling index

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Swelling index ofdefferent ratio sodium alginate microsphere

Table NO.22: Swelling index of defferent ratio sodium alginate microsphere

Formulation	Swelling index
MS1	78.3
MS2	86.3
MS3	83.5
MS4	84.0

The four formulations are prepared using different polymer ratio were evaluated. The swelling index range for all the formulation were founded to be 72.5-89.0. The formulation MS4 which contain1:2 drug polymer ratio showed higher swelling index 89.0 %.

In-Vitro Release Studies

The foundation formulation for all 12 solid dispersion formulations was a solid dispersion with a drug: polymer ratio of 1:1. Four distinct formulations were created by incorporating the improved solid dispersion formulation (F10) into microspheres. All formulations are tested at pH 1.2 HCl, but due to enteric coating, there is no drug release. These formulations are subsequently tested at pH 6.8 phosphate buffer. The best formulation, MS2, included 1 gm of solid dispersion and demonstrated maximum drug release from formulation to formulation, as seen in fig. 11.28,29

Table NO.23: Percentage cumulative release of different of Cefpodoxime proxetil microshpere formulations in phosphate buffer (pH 6.8)

Time interval (hrs)	Percentage drug relase of different formulation 8 hrs			
	MS_1	MS_2	MS_3	MS_4
0	0	0	0	0
0.5	37.42	42.73	39.04	40.12
1	43.67	47.55	44.40	46.67
2	47.75	52.52	50.51	51.34
3	51.18	59.44	56.10	55.11
4	55.74	66.58	65.07	59.26
5	60.45	74.46	71.97	64.08
6	67.93	82.52	77.48	68.31
7	72.45	93.75	84.12	70.15
8	82.86	97.89	86.10	72.02

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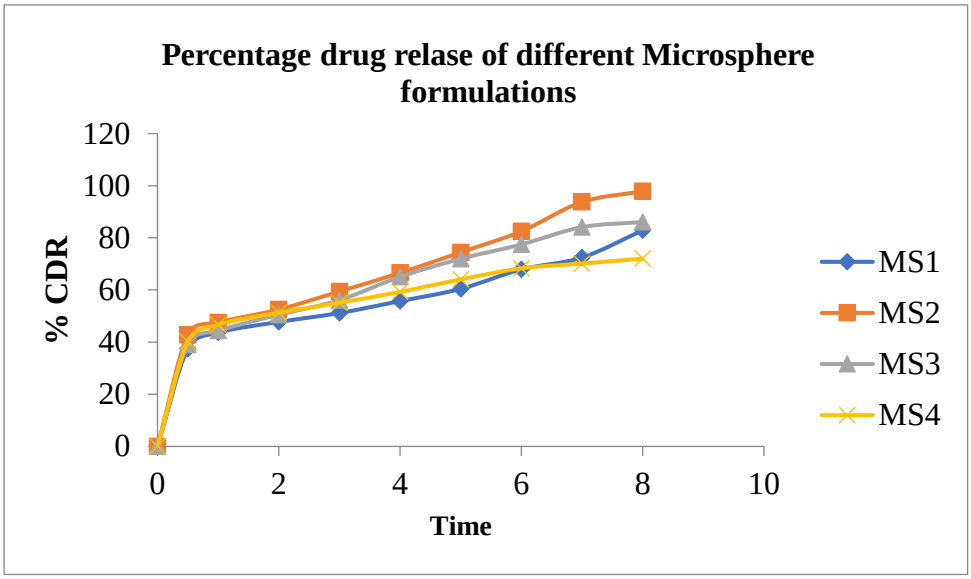

Figure-12:- Comparative dissolution profile of cefpodoximeproxetil solid

The four formulations are prepared using different polymer ratio were evaluated. The formulation MS2 which contain 1:1 drug polymer ratio showed higher % CDR as showed in fig. 12.

Scanning Electron Microscopy (SEM):- The microspheres were founded smooth surface and the size less than10µm by SE.

Table NO.24: The Formulation's Stability Studies at room temp (pH-6.8)

S.No	Number of day	Percentage Drug Remaining			
		MS1	MS2	MS3	MS4
1	0	98.59	98.95	98.98	98.97
2	15	58.52	98.91	98.85	98.87
3	30	98.51	98.82	98.72	98.75
4	45	98.46	98.75	98.62	98.65
5	60	98.35	98.68	98.53	98.52
6	75	98.08	98.58	98.41	98.43
7	90	98.06	98.51	98.35	98.27
8	105	98.05	98.46	98.24	98.24
9	120	98.03	98.38	98.18	98.19

CONCLUSION

The current study set out to create solid dispersions utilising PEG-4000, PEG-6000, mannitol, and -cyclodextrin in order to improve the solubility and, subsequently, the dissolving behaviour of the drug Cefpodoxime proxetil. The solvent evaporation method was used to make solid dispersions, and it produced effective results with high drug content and notably improved drug

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water solubility. After using the ionic gelation procedure to produce the mucoadhesive microspheres, the ideal solid dispersion formulation was applied. These microspheres were coated with enteric coating polymer to protect the formulation from the extremely acidic environment of the stomach. The resulting cefpodoxime proxetil mucoadhesive microspheres exhibited a better drug release profile and released the medicine gradually over time. In accordance with the aforementioned study, solid drug dispersion increases drug solubility, and mucoadhesion of the microspheres causes sustained drug administration, which boosts therapeutic efficacy and reduces dosing frequency while increasing patient compliance with the medication.

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