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Formulation, Characterization and Comparison of Cefaclor and Cefdinir Microspheres

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Abstract
The purpose of this research work is to increase and compare the residence time of drugs Cefaclor and Cefdinir by formulating as floating microspheres and to study the effect of formulation variables on microspheres characteristics. Microspheres are prepared by solvent evaporation method. For each drug nine different formulations are prepared by changing drug to polymer ratio, volume of internal phase, volume of external phase and stirring time. The prepared microspheres are characterized for drug - polymer compatibility by IR, percentage yield, particle size analysis, drug entrapment efficiency, and surface morphology by SEM, bulk density, percentage buoyancy, in-vitro release and release kinetic studies. Results of these evaluations showed that particle size in the range of 100.8±1.6 µm to 106.2±1.3µm, and102.1±1.3 to 108.6±1.7 entrapment efficiency is found to be 75.72±1.94 to 92.02±1.07% and 75.69±1.91 to 89.45±1.63% and drug content is found to be in the range 95.55±1.4 to 99.92±2.67 and 96.89±2.1 to 99.11 ± 2.1 respectively. Fourier-Transform Infra-Red (FT-IR) studies ensured that no drug - polymer interaction in the formulated microspheres is found. The surface topography revealed a spherical surface for all the formulations and a round cavity enclosed by an outer shell composed of the drug and polymer. In- vitro release profile of microspheres for F14 and F23 formulations are found to be 98.45±0.47 and 99.87±0.36 at the end of 12hrs. In release kinetic studies, the F14 and F23 formulations followed zero order and first order drug release with non-Fickian diffusion mechanism.

Keywords
Cefaclor, Cefdinir, FT-IR, SEM, Microspheres.

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INTRODUCTION
Microspheres are defined as solid spherical particles containing dispersed drug in either solution or microcrystalline form. They are ranging in size from 1 to 1000 micrometer. Microspheres are in strict sense, spherical solid particles. Microcapsules are small particles that contains an active agent as a core material and coating agent as shell, at present there is no universally accepted size range that particle must have in order to be classified as microcapsules. However, many workers classified capsules smaller than 1 micrometer as nano capsules and capsules layer more than 1000 micrometer as macro particles. Commercial microcapsules typically have a diameter

between 3-80 micrometer and contain 10-90 weight % cores. Cefaclor and Cefdinir are second generation and third cephalosporin antibiotic drugs. The bioavailability of the above mention drugs is well absorbed with a half-life of 0.6-0.9 hour and 1.7 to 0.6 hour respectively. To increase the bioavailability of the Cefaclor and Cefdinir with reducing dosage frequency microspheres are selected as suitable approach.

MATERIAL AND METHODS

Materials: Cefaclor and Cefdinir are obtained as a gift samples from Hetero drugs, Hyderabad (India). SCMC, HPMCK4M, EUDRAGIT are obtained from Colorcon India Pvt.Ltd, Ethanol, DCM, Tween80, Liquid paraffin are purchased from Colorcon India Pvt. Ltd. All other chemicals and reagents used are of analytical grade.

Preparation of Cefaclor and Cefdinir individual Microspheres by non-aqueous solvent evaporation technique:

Microspheres containing Cephalosporin drugs as a core material are prepared by a non- aqueous solvent evaporation method. Drug and different polymer ratio are mixed in the mixture of dichloromethane and ethanol at a 1:1 ratio. The slurry is slowly introduced into 30 ml of liquid paraffin containing 0.01% Tween 80, while stirring at 1200 rpm using a mechanical stirrer equipped with three bladed propellers at room temperature. The solution is stirred for 2 h and the solvent evaporates completely and filtered by using filter paper. The microspheres obtained are washed repeatedly with petroleum ether (40-60 °C) until free it is from oil. The collected microspheres are dried at room temperature and subsequently stored in desiccators.

Physical characterization of microspheres:

Solubility study: Excess drug is added carefully using a spatula to 10 ml of the media in a conical flask, while stirring until a heterogeneous system (solid sample and liquid) is obtained. The solution containing excess solid is then capped and stirred at 150 rpm at room temperature for 24 hours. The solution containing excess solid is filtered using 0.45µm PVDF filter, appropriate dilutions are then made and analyzed using UV spectrophotometer at required nanometer range of drug. The same procedure is fallowed for all selected drugs. (Saturation solubility is carried out at 25 ^{0}C using required different buffers).

Determination of absorption maximum (λ_{max}): The wavelength at which maximum absorption of radiation takes place is called as λ_{max}. This λ_{max} is characteristic or unique for every substance and useful in identifying the substance. For accurate analytical work, it is important to determine the absorption maxima of the substance under study. Most drugs absorb radiation in ultraviolet region (190-390nm), as they are aromatic or contain double bonds.

Accurately weighed 100mg of drug is dissolved in pH 6.8 buffer taken in a clean 100 ml volumetric flask. The volume is made up to 100ml with the same which will give stock solution-I with concentration 1000µg/ml. From the stock solution I, 5ml is pipette out in 50ml volumetric flask. The volume is made up to 50ml using pH 6.8 buffer to obtain stock solution-II with a concentration 100µg/ml. From stock solution-II, 1ml is pipette out in 10ml volumetric flask. The volume is made up to 10ml using pH 6.8 buffer to get a concentration of 10µg/ml. This solution is then scanned at 200-400nm in UV-Visible double beam spectrophotometer to attain the absorption maximum (λ-$_{max}$).

PREPARATION OF CALIBRATION CURVE

Procedure for standard curve in pH 6.8:

10 mg of drug is dissolved in 10 ml of pH 6.8 by slight shaking (1000 mcg/ml). 1 ml of this solution is taken and made up to 20 ml with pH 6.8, which gives 20 mcg/ ml concentration (stock solution). From the stock solution, concentrations of 5, 10, 15, 20 and 25 µg/ml in pH 6.8 are prepared. The absorbance of dilute solutions is measured at particular nanometer and a standard plot is drawn using the data obtained. The correlation coefficient is calculated.

FTIR analysis:

The drug-polymer interactions are studied by FTIR spectrometer, Shimadzu 8400 S. 2% (w/w) of the sample, with respect to a potassium bromide (KBr; SD Fine Chem. Ltd., Mumbai, India) is mixed with dry KBr. The mixture is ground into a fine powder using mortar and then compressed into a KBr discs in a hydraulic press at a pressure of 10000 PSI. Each KBr disc is scanned 10 times at a resolution of 2 cm–1 using Happ-Genzel apodization. The characteristic peaks are recorded.

MICROMERETIC PARAMETERS:

Bulk Density:

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. It is determined by pouring pre-sieved blend into a graduated cylinder via a large funnel and measure the volume and weight as is given by

Bulk density= weight of blend/Bulk volume

Tapped density:

Tapped density is determined by placing a graduated cylinder containing known mass of blends on a mechanical tapped apparatus, which is operated for

a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed.

Tapped density=weight of blend/tapped volume of blends

Compressibility Index:
The compressibility index of the granules was determined by Carr's compressibility index.

Carr's index (%) = [(TBD – LBD) × 100]/TBD

Hausner's ratio:
Hausner's ratio is determined as the ratio between the tapped density to that of the bulk density.

H.R = Tap Density / Bulk Density

Angle of repose:
The manner in which stresses are transmitted through a bed and beds response to applied stress is reflected in the various angles of friction and response. The most commonly used of these is angle of repose, which may be determined experimentally by a number of methods. The method used to find the angle of repose is to pour the powder in a conical heap on a level flat surface and measure the inclined angled with the horizontal pile.

$\theta = \tan^{-1}(h/r)$

Particle Size:
It is possible to use ordinary microscope for particle size determination in the range of 0.2 to above100 µm to measure particle size of individual microsphere. All the microspheres are evaluated with respect to their size and shape using optical microscope fitted with an ocular micrometer and a stage micrometer. Ocular micrometer is calibrated with the stage micrometer. Slides of dilute suspensions of microspheres in liquid paraffin are prepared and slides are placed on mechanical stage of microscope. The diameter of 100 microspheres is measured randomly by optical microscope and average particle size is determined.

Scanning electron microscopy (SEM):
In the pharmaceutical industry, SEM may be used as a qualitative tool for the analysis of drug substance and drug product in order to obtain information on the shape and surface structure of the material. SEM plays an important role in the characterization of nanoscale and sub-micron particles. It has been used to determine surface topography, texture and to examine the morphology of fractured or sectioned surfaces. The examination of the surface of polymeric drug delivery systems can provide important information about the porosity and microstructure of device.

Actual drug content and entrapment efficiency:
10 mg of microspheres are accurately weighed and transferred in a 50 ml volumetric flask. Volume is adjusted with 1% SLS and microspheres are dissolved by ultra-sonication for 3 h at 25 °C. The samples are filtered through 0.2 µm membrane filter. 5 ml from the sample solution is transferred to 50 ml volumetric flask and volume is adjusted to 50 ml with same medium and absorbance of samples are measured at 288 nm using UV-spectrophotometer. Actual drug content (AC) and encapsulation efficiency (EE) are calculated using following equations. All analyses are carried out in triplicate.

$$AC(\%) = \frac{Cact}{Cms} \times 100$$

$$EE(\%) = \frac{Cact}{Cthe} \times 100$$

Where, Cact= Actual drug content in microspheres
Cms= Weighed quantity of microspheres
Cthe= Theoretical quantity of drug in microspheres calculated from the quantity added in the process.

***In-vitro* Dissolution Studies:**
The dissolution test measures the amount of time required for certain percentage of the drug substance in a tablet to go into solution under a specified set of conditions. It describes a step towards physiological availability of the drug substance, but it is not designed to measure the safety or efficacy of the formulation being tested.

RELEASE KINETIC MODELS:
To analyze the mechanism for the drug release and drug release rate kinetics of the dosage form, the data obtained is fitted in to Zero order, First order, Higuchi matrix, Kersmeyers-Peppas and Hixson Crowell model. In this by comparing the R^2-values obtained, the best-fit model is selected.

Stability studies:
Stability studies are conducted for the upgrade formulation confirmed from the in vitro dissolution data, for Particle size, % Yield, Entrapment efficiency, and % Drug content at 40°C /75%RH for a period of 3 months.

RESULTS AND DISCUSSION

Preparation of microspheres*:* Microspheres are prepared by solvent evaporation method. Many of the researchers employed with solvent evaporation method due to its simplicity and reproducibility. The

solubility of Cefaclor and Cefdinir are very poor in water (0.52mg/ml and 0.14 mg/ml) and in 0.1N HCl (0.072mg/ml and 0.020mg/ml) respectively. The solubility of Cefaclor and Cefdinir increased with increase in pH 6.8 of the buffer from 0.39 to 1.88 mg/ml and 0.79 to 1.26 mg/ml respectively.

Solvent combination: Selection of solvent is very important for microspheres preparation. A mixture of ethanol and dichloromethane used for this microsphere's preparation as solvent. Because when dichloromethane used alone the polymer get precipitated rapidly at the time of mixing with water. So, ethanol is added to that solvent. During microspheres formation ethanol gets diffused into the water and dichloromethane is evaporated.

Determination of absorption maxima (λ_{max}) of CEFACLOR and CEFDINIR:

The maximum absorbance of the Cefaclor and Cefdinir in pH 6.8 is found to be 268nm and 282nm respectively as shown in Fig. Hence, the wavelength of 268nm and 282nm are selected for analysis of drug in dissolution media.

Standard curve of Cefaclor and Cefdinir:

A linear relationship is observed between concentrations of drug solution in pH 6.8and absorbance, over the concentration range of 5-25µg/mL. The coefficient of correlation (R^2) is found to be 0.9990, indicating that the drugs solutions obeying Beer's- Lambert law in the concentration range of 5-25µg/ml. Hence it is concluded that dissolution samples can be analyzed in 0.1N HCl by measuring absorbance at 286nm and 268nm using UV-Visible Spectrophotometer.

FTIR Studies:

The Cefaclor and Excipients, Cefdinir and Excipients interactions are studied by comparing the FTIR spectrum of the optimized blend with that of Cefaclor and Cefdinir pure drug as shown in Fig. The comparison study demonstrates that there is no interaction between the drug and other ingredients of the formulation including Excipients such as HPMC, Eudragit and SCMC as shown in Fig, thus revealing compatibility of the selected drug with the excipients.

MICROMERETIC PARAMETERS:

The flow properties of Cefaclor F10-F18 formulations like bulk density, tapped density, compressibility index and Hausner's ratio are found to be 0.432±0.14 gm/cc to 0.520±0.14 gm/cc, 0.478±0.88 gm/cc to 0.587 ± 0.23 gm/cc,8.77 ± 0.85% to 13.17 ± 0.25% and 1.09 ± 0.30 to 1.15 ± 0.89 and for Cefdinir F19-F27 formulations 0.51 ± 0.25 gm/cc to 0.59 ± 0.07 gm/cc, 0.62 ± 0.62 gm/cc to 0.69 ± 0.14 gm/cc,7.936 ± 0.19% to 22.58 ± 0.56% and 1.086 ± 0.56 to 1.301 ± 0.19 respectively. The observed values are within I.P limits and also exhibit good flow character for the improved formulation.

Particle Size The particle size of the formulations F-10 to F-18 and F19-F27 is found to be in the ranges from 100.8 ± 1.6µm to 106.2±1.3µm and 102.1 ± 1.3 to 108.6 ± 1.7 respectively.

Scanning electron microscopy analysis (SEM)

The optimized formulations are evaluated for its surface morphology by using Scanning electron microscopy. The outer surface of the microspheres is found to be smooth. The surface topography revealed a spherical surface for all the formulations and a round cavity enclosed by an outer shell composed of the drug and polymer. The particle size is found to be 100µm.

Actual drug content and entrapment efficiency

The entrapment efficiency and actual drug content of the Cefaclor formulations F-10 to F-18 are 75.72±1.94 to 92.02 ± 1.07% and 95.55 ± 1.4 to 99.92 ± 2.67 respectively and for Cefdinir formulations F19 to F27 are 75.69 ± 1.91 to 89.45 ± 1.63% and 96.89 ± 2.1 to 99.11 ± 2.1 respectively.

***In-vitro* dissolution studies of Cefaclor and Cefdinir:**

The formulations of Cefaclor F10- F12 and Cefdinir F19 to F21 prepared with (ratios range 1:1, 1:1.5, 1:2) concentration of polymer like SCMC and drug release are shown in Table. As the polymer concentration decreases the drug release increases. This is due to insufficient entrapment of the drug formulations containing low concentration of hydrophilic polymer (SCMC).

The formulation of Cefaclor F10 and Cefdinir F19showed burst effect and released 100.23±0.74% and100.18±0.18% at the end of 6hrs respectively. The formulations of Cefaclor F11 and F12and Cefdinir F20 and F21 drug release is 99.46±0.30%, 97.73±0.70 and 98.98±0.59%, 99.23±0.51 at the end of 8 and 10 hrs respectively due to increase of the polymer concentration. In the case of formulations F12 and F21 as polymer concentration further increases (1:2) drug release is decreased.

The formulations of Cefaclor F13 and Cefdinir F22 releases 99.23±0.64% and 99.85±0.79 the end of 8 hrs and 6 hrs respectively. Formulations of Cefaclor F14 and F15 release 98.45±0.47% & 80.45±0.87 and Cefdinir F23 and F24 99.87±0.36 and 89.99±0.48 at the end of 12hrs respectively. Because of the HPMC (high viscosity and high molecular weight) upon contact with dissolution medium swelling occurs due to the disruption of hydrogen bonding among the polymeric chains and forms a thick gel layer on the surface, which gets eroded over period of time. Thus,

this parameter is responsible for sustained/controlled drug release rate.

The formulations of Cefaclor F16, F17 and F18 and Cefdinir F25, F26 and F27are tried with Eudragit (ratios range 1:1, 1:1.5, 1:2) as retardant being insoluble in gastric pH. The formulations F16 and F25 are found to be 82.45±0.65 and 70.89±0.15 at the end of 12hrs due to low polymer concentration. F17, F18 and F26, F27 showed better control on drug release than other formulations and also exhibited incomplete drug release which might be due to hydrophobic polymer (Table and Fig).

The formulation of Cefaclor F14 and Cefdinir F23 are made with the HPMC in the drug polymer ratio of 1:1.5 drug releases are found to be 98.45±0.47% and 99.87±0.36 at the end of 12hrs with best drug release pattern. The reason for this fact might be the formation of thick gel layer by matrices around the surface that delays diffusion and release of drug, thus F14 of Cefaclor and F23 of Cefdinir are considered as optimized formulations.

RELEASE KINETIC MODELS:

The optimized formulation of Cefaclor F14 had coefficient of determination (R^2) values of Zero order, First order, Higuchi and Korsmeyer Peppas of 0.9540, 0.7640, 0.977 and 0.959 and formulation of Cefdinir F23 is 0.874, 0.931, 0.971 and 0.964 respectively. A good linearity is observed with the zero order and first order respectively. The slope of the regression line from the Higuchi plot indicates the rate of drug release through mode of diffusion, and further confirms the diffusion mechanism. The data fitted into the Korsmeyer Peppas equation which showed linearity with slope n value of 0.493 for upgrade formulation F14 and 0.515 for optimized formulation F23. These n values indicate the coupling of (swelling, polymer relaxation) diffusion and erosion mechanism. This type of drug release is called anomalous diffusion. Thus, it indicates that the drug release from the tablet follows non-Fickian diffusion mechanism. The presence of swelling and cross-linked polymers within the matrix structure might be responsible for the drug release controlled by more than one process. Thus, with regard to release kinetics, the optimized batch F14 and F23 best fits into peppas model and shows zero order and first order drug release with non-Fickian diffusion mechanism respectively.

Stability studies of optimized formulation F14 and F23:

Stability studies are conducted for Particle size, %Yield, Entrapment efficiency, & % Drug content and confirmed that there is no significant change in the parameters of optimized formulation at storage condition of 40°C ± 2°C / 75 ± 5 %RH after 6 months.

CONCLUSION

In this research work an attempt is made to increase the bioavailability of the Cefaclor and Cefdinir with reducing dosage frequency microspheres. Formulations are successfully made and *in–vitro* evaluation of shows encouraging results. By these evaluations following statement can be concluded (i) No interaction between the drug and polymer is confirmed. (ii) The desired yield and entrapment efficiency are obtained. (iii) It provides sustained release of drug over more than 12 hours. (iv) Drug release from microspheres follows zero order and first order drug release with non-Fickian diffusion mechanism. (v) The drug: polymer ratio has significant effect on the all characteristics of microspheres, but other variables have effect only on a few characteristics of the microspheres.

Table1: Formulation design of Cefaclor Microspheres:

Sl.no	Ingredients	F10	F11	F12	F13	F14	F15	F16	F17	F18
1	CEFACLOR (gm)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
2	SCMC (gm)	1	1.5	2	-----	------	------	------	------	------
3	HPMCK4M (gm)	------	------	------	1	1.5	2	------	------	------
4	EUDRAGIT (gm)	------	------	------	------	------	------	1	1.5	2
5	Ethanol (ml)	6	10	12	15	20	23	10	15	20
6	DCM (ml)	6	10	12	15	20	23	10	15	20
7	Tween(ml)	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
8	Liquid paraffin (ml)	90	90	90	90	90	90	90	90	90

Table 2: Formulation design of Cefdinir Microspheres:

Sl.No	Ingredients	F19	F20	F21	F22	F23	F24	F25	F26	F27
1	CEFDINIR	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
2	SCMC (gm)	1	1.5	2	-----	------	------	------	------	------
3	HPMCK4M	------	------	------	1	1.5	2	------	------	------
4	EUDRAGIT (gm)	------	------	------	------	------	------	1	1.5	2
5	Ethanol (ml)	6	10	12	15	20	23	10	15	20
6	DCM (ml)	6	10	12	25	20	23	10	15	20
7	Tween(ml)	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
8	Liquid paraffin (ml) paraffin (ml)	90	90	90	90	90	90	90	90	90

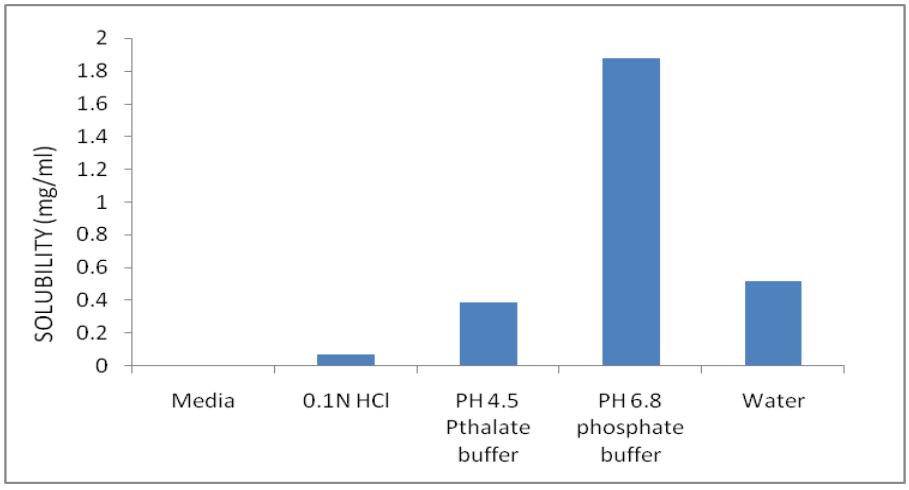

Fig 1: **Saturation solubility of CEFACLOR**

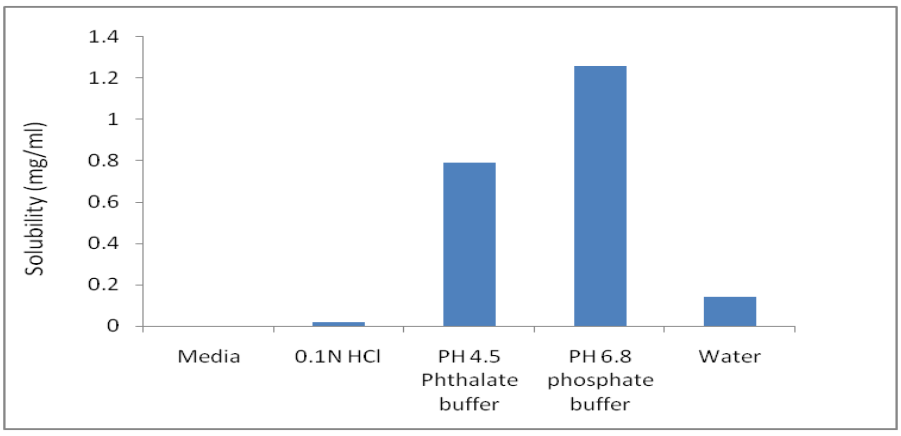

Fig 2: **Saturation solubility of CEFDINIR**

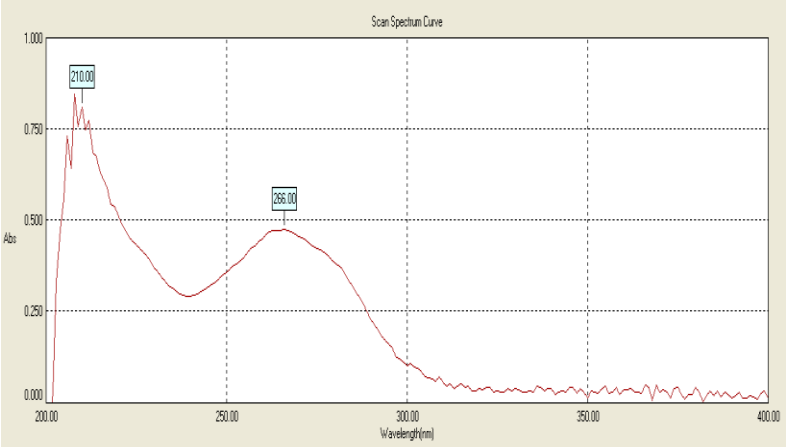

Fig: 3 Determination of absorption maxima of Cefaclor

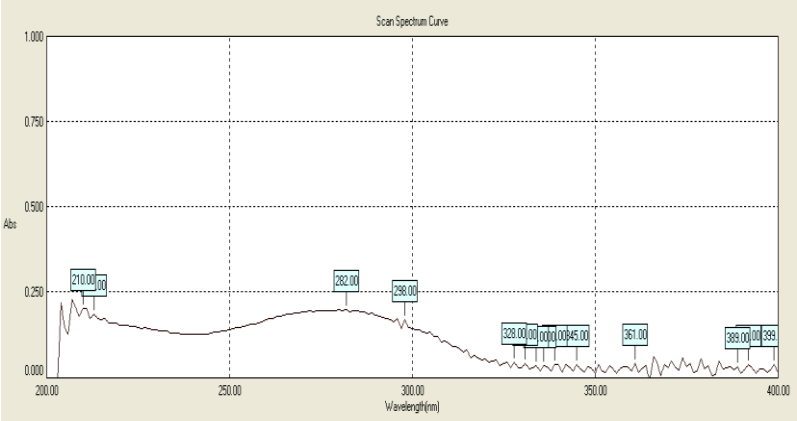

Fig: 4 Determination of absorption maxima of Cefdinir

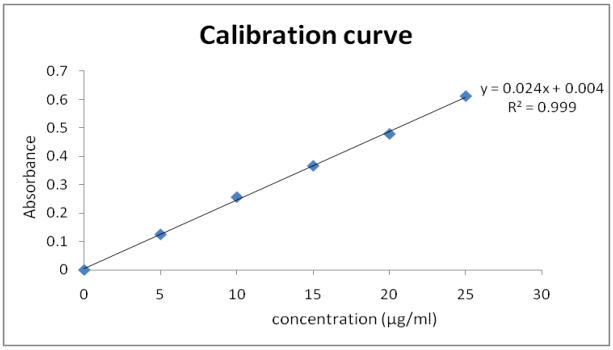

Fig5: Standard curve of CEFACLOR in PH6.8(λ_{max268})

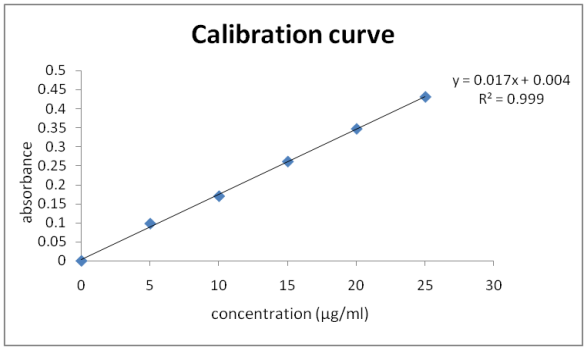

Fig6: Standard curve of CEFDINIR in PH6.8(λ_{max282})

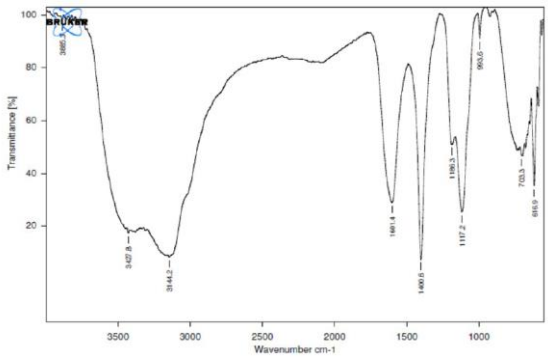

Fig 7: FTIR of CEFACLOR

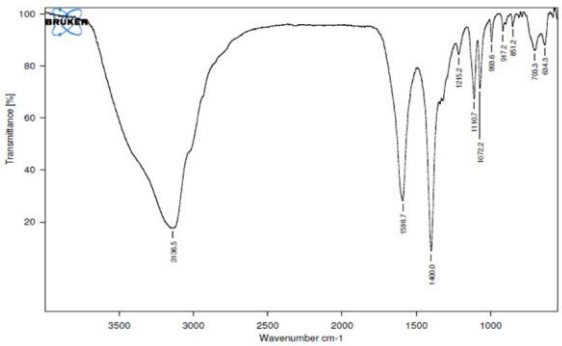

Fig 8: FTIR of CEFDINIR

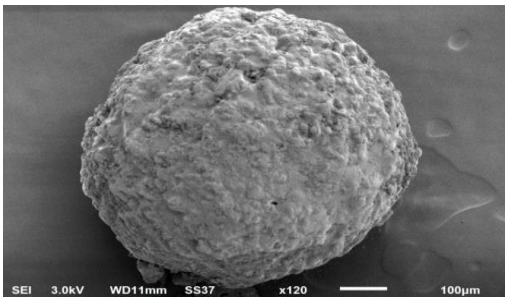

Fig 9: SEM analysis of CEFACLOR

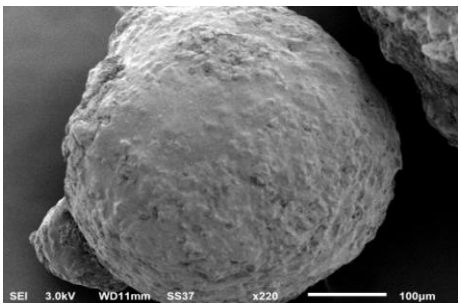

Fig 10: SEM analysis of CEFDINIR

Table: 3 Characterization of CEFACLOR and CEFDINIR microspheres

Cefaclor Formulations	Bulk Density	Tapped Density	Hausner's Ratio	Compressibility Index	Cefdinir Formulations	Bulk Density	Tapped Density	Hausner's Ratio	Compressibility Index
F10	0.516±0.55	0.587±0.23	1.13±0.16	12.09±0.47	F19	0.57±0.14	0.63±0.07	1.105±0.01	9.523±0.75
F11	0.520±0.14	0.570±0.66	1.09±0.30	08.77±0.85	F20	0.53±0.78	0.64±0.12	1.207±0.15	17.18±0.48
F12	0.487±0.58	0.546±0.50	1.12±0.07	10.80±0.21	F21	0.51±0.25	0.62±0.62	1.215±0.36	17.74±0.89
F13	0.455±0.25	0.501±0.44	1.10±0.60	9.18±0.14	F22	0.54±0.09	0.68±0.71	1.259±0.78	22.58±0.56
F14	0.448±0.78	0.516±0.36	1.15±0.89	13.17±0.25	F23	0.52±0.63	0.64±0.33	1.230±0.41	18.75±0.78
F15	0.510±0.07	0.568±0.14	1.11±0.55	10.21±0.61	F24	0.58±0.69	0.63±0.45	1.086±0.56	7.936±0.19
F16	0.476±0.15	0.526±0.22	1.10±0.23	9.50±0.55	F25	0.53±0.57	0.69±0.14	1.301±0.19	23.18±0.51
F17	0.515±0.66	0.570±0.01	1.10±0.08	9.64±0.14	F26	0.59±0.07	0.67±0.30	1.135±0.02	19.40±0.41
F18	0.432±0.14	0.478±0.88	1.10±0.12	9.62±0.05	F27	0.55±0.10	0.66±0.21	1.2±0.11	16.66±0.05

Table 4: Particle size, Drug Entrapment Efficiency of Cefaclor and Cefdinir microspheres

Cefaclor Formulations	Particle Size (µm)	% Yield	Entrapment Efficacy	Drug Content	Cefdinir Formulations	Particle Size (µm)	% Yield	Entrapment Efficiency	Drug Content
F10	102.1±1.3	87.82±2.01	78.68±2.1	97.65±1.6	F19	103.4±1.42	92.70±1.19	85.04±1.87	97.59±1.97
F11	102.9±1.4	85.95±1.98	76.87±1.91	96.89±2.1	F20	102.5±1.3	85.95±1.98	76.87±1.91	98.64±2.01
F12	101.9±1.7	94.82±2.16	88.35±2.67	98.28±1.7	F21	103.2±0.9	94.82±2.16	89.45±1.63	98.46±3.22
F13	104.2±1.2	86.90±2.45	75.72±1.94	98.73±1.9	F22	103±2.8	86.90±3.05	75.69±1.91	98.78±1.4
F14	105.1±1.5	93.55±1.37	86.68±2.08	97.89±1.92	F23	108.6±1.7	93.25±1.37	86.98±2.08	99.11±2.1
F15	106.2±1.3	85.35±1.98	76.84±1.98	98.48±2.08	F24	106±2.35	84.62±1.01	76.68±2.1	97.46±2.4
F16	101.8±1.1	86.27±2.05	76.68±2.12	99.24±1.91	F25	103.8±1.8	93.70±1.28	87.04±1.92	98.95±1.8

F17	100.8±1.6	98.70±1.87	92.02±1.07	99.92±2.67	F26	102.1±1.3	87.82±2.01	78.68±2.1	97.75±1.5
F18	101.1±1.1	85.82±2.01	88.68±1.1	95.55±1.4	F27	102.9±1.4	85.95±1.98	76.87±1.91	96.89±2.1

Table 5: Dissolution profile of CEFACLOR formulations (Mean±SD; n=6)

Time(hr)	F10	F11	F12	F13	F14	F15	F16	F17	F18
0	0	0	0	0	0	0	0	0	0
1	38.82 ±0.71	30.23 ±0.40	28.89 ±0.14	35.69 ±0.12	28.23 ±0.34	15.23 ±0.10	20.12 ±0.49	13.35 ±0.10	12.21 ±0.82
2	63.45 ±0.45	54.23 ±0.36	38.23 ±0.33	50.23 ±0.05	36.53 ±0.54	28.23 ±0.22	32.43 ±0.12	18.54 ±0.45	18.15 ±0.09
4	84.46 ±0.41	70.63 ±0.12	49.99 ±0.52	67.74 ±0.47	43.45 ±0.10	39.42 ±0.84	44.52 ±0.30	27.84 ±0.36	24.23 ±0.79
6	100.23 ±0.74	81.23 ±0.55	68.89 ±0.74	82.12 ±0.59	59.53 ±0.06	48.86 ±0.74	51.23 ±0.78	45.57 ±0.71	29.47 ±0.56
8	---	99.46 ±0.30	83.45 ±0.02	99.23 ±0.64	71.25 ±0.40	60.99 ±0.65	63.33 ±0.04	53.84 ±0.05	38.89 ±0.34
10	---	---	97.73 ±0.70	---	83.45 ±0.20	73.45 ±0.02	75.23 ±0.25	59.99 ±0.89	49.98 ±0.10
12				---	98.45 ±0.47	80.45 ±0.87	82.45 ±0.65	65.54 ±0.70	59.98 ±0.54

Table 6: Dissolution profile of CEFDINIR formulations (Mean±SD; n=6)

Time(hr)	F19	F20	F21	F22	F23	F24	F25	F26	F27
0	0	0	0	0	0	0	0	0	0
1	40.85 ±0.56	33.32 ±0.30	26.89 ±0.91	38.91 ±0.14	25.12 ±0.02	19.87 ±0.18	10.53 ±0.65	8.45 ±0.19	7.23 ±0.09
2	71.35 ±0.46	57.53 ±0.18	49.85 ±0.87	64.85 ±0.36	39.42 ±0.79	30.24 ±0.55	19.83 ±0.49	15.45 ±0.97	14.18 ±0.57
4	91.52 ±0.57	73.85 ±0.42	67.23 ±0.79	86.35 ±0.45	46.8 ±0.58	44.89 ±0.17	25.35 ±0.87	21.23 ±0.56	19.98 ±0.18
6	100.18 ±0.18	85.85 ±0.07	79.99 ±0.63	99.85 ±0.79	55.23 ±0.36	58.87 ±0.45	37.45 ±0.96	32.35 ±0.39	27.46 ±0.96
8	---	98.98 ±0.59	84.55 ±0.42	---	69.98 ±0.47	67.54 ±0.32	42.54 ±0.74	39.01 ±0.47	32.24 ±0.87
10	---	---	99.23 ±0.51	---	85.54 ±0.28	79.86 ±0.14	58.87 ±0.58	50.08 ±0.52	46.64 ±0.11
12				---	99.87 ±0.36	89.99 ±0.48	70.89 ±0.15	62.15 ±0.87	57.98 ±0.89

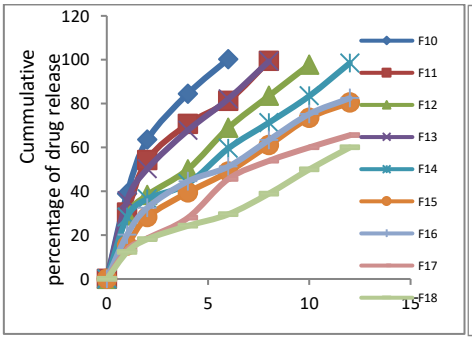

Fig 11: *In-vitro*dissolution profile of CEFACLOR

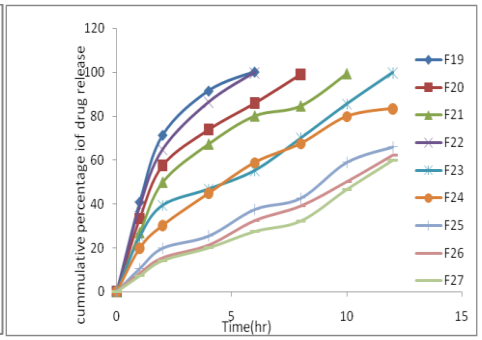

Fig 12: *In-vitro*dissolution profile of CEFDINIR

Table7: Stability data of CEFACLOR and CEFDINIR optimized formulations (F14) and (F23) physico-chemical parameters

Parameter	Initial For Cefaclor F14	For F14 After 3months At 40^0c/75%RH	For F14 After 6months At 40^0c/75%RH	Initial For Cefdinir F23	For F23 After 3months At 40^0c/75%RH	For F23 After 6months At 40^0c/75%RH
Particle size	105.1± 1.5	105.20± 0.87	105.12± 1.8	108.6± 1.7	108.45± 1.06	108.3± 1.23
% Yield	93.55±1.37	93.47±1.08	93.45±1.20	93.25±1.37	93.14±1.01	93.21±1.41
Entrapment efficiency	86.68±2.08	86.50±2.41	86.79±1.56	86.98±2.08	86.56±1.89	86.90±2.01
% Drug content	97.89±1.92	97.74±1.08	97.92±1.54	99.11±1.57	99.09±1.04	99.03±1.78

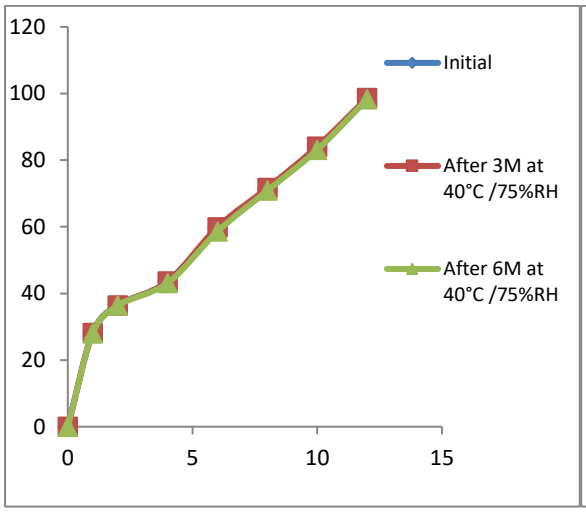

Fig 13: Optimized formulation of CEFACLOR (F14) *in-vitro* dissolution at 40°C /75%RH

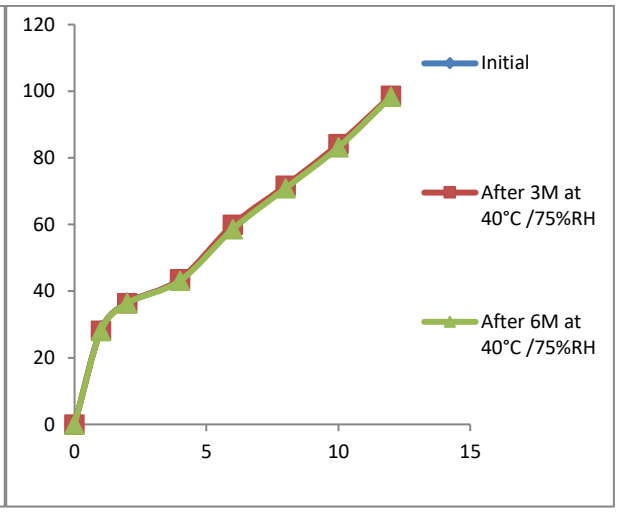

Fig 14: Optimized formulation of CEFDINIR (F23) *in-vitro* dissolution at 40°C /75%RH

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