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FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLET OF CEFIXIME USING MUCILAGE OF MIMOSA PUDICA SEED

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ABSTRACT

The objective of the present investigation was to develop a sustained release tablet of Cefixime by the wet granulation technique using a combination of mucilage of mimosa pudica seed. Different batches of Cefixime sustained release tablets were prepared by using microcrystalline cellulose as disintegrant agent by wet granulation technique. The compatibility of the drug and excipients was done by thin layer chromatography, results were found to be compatible. Granules of prepared batches were evaluated for their physical properties and found to be good and satisfactory. Tablets were evaluated for various physicochemical parameters like hardness (5.33±0.2), thickness (4.7±0.05), friability (4.14±0.9), weight variation test (670±4.47), swelling index (40.79±0.8) in 6 hour, drug content (99.25±0.8), and *in-vitro* drug release 98.51±0.8 in 12 hour. To study the effect of concentration of mucilage on drug release from SR tablets, 3^2 full factorial design was applied. The concentration of mucilage and microcrystalline cellulose were used as independent variables, while percentage drug release at 1 h and 12 h were selected as the dependent variable. Formulation F5 was showing the highest sustaining action so this formulation was selected for further study. Drug release of optimized F5 batch was found 98.51% which was found within 12 hours. In order to formulate sustained release tablet, cefixime was mixed with mucilage and other excipient. Drug content in formulation F5 were found to be 99.25% and which sustained the release of

drug for 12 hours. Hence it can be concluded that this formulation can be employed to retard the release of drug.

KEYWORDS: Cefixime; Sustained release; Mucilage; Microcrystalline.

INTRODUCTION

Sustained release is the terms used to identify drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period after administration of single dose of the drug.

The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve instantly and then maintain the desired drug concentration.[1,2]

These preparations provide an immediate dose required for the normal therapeutic response, followed by the gradual release of drug in amounts sufficient to maintain the therapeutic response for a specific extended period of time. The major advantage of this category is that, in addition to the convenience of reduced frequency of administration, it provides blood levels that are devoid of the peak-and-valley effect which are characteristic of the conventional intermittent dosage regimen.[3] Sustained release dosage forms are designed to complement the pharmaceutical activity of the medicament in order to achieve better selectivity and longer duration of action.[4]

Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. Sustained release formulation maintains a uniform blood level of drug with better patient compliance as well as increased efficacy of drug.[5] Sustained release tablets are generally taken once or twice a day during a course of treatment whereas in conventional dosage forms there is need to take 3-4 times dosage in a day to achieve the same therapeutic action.[6]

Mimosa pudica L. is a creeping annual or perennial herb. It has been identified as mimosa pudica in Ayurveda and has been found to have antiasthmatic, antifertility activity, diuretic activity, antidiarrheal active, analgesic, and antidepressant properties. Mimosa pudica is known to possess sedative and tonic properties, and has been used traditionally in the

treatment of various ailments including alopecia, diarrhea, dysentery, insomnia, tumor, and various urogenital infections. The decoction of the whole plant is used in vaginosis, tooth ache, urinary tract infection, and infections in the lower genital tract of female. Phytochemical studies on M. pudica have presence of alkaloids, flavonoids C-glycosides, non-protein amino acid, sterols, tannins, terpenoids and fatty acids [7]. Seeds contain mucilage composed of d-xylose and d-glucoronic acid, yielding 17% greenish yellow fatty oil. In folk medicine, M. pudica roots are used for diuretic activity and the treatment of many other complications. Urinary tract infections are treated by a decoction of leaves. M. pudica seed is used to treat urinary tract infection.

Cefixime is an antibiotic, it is a third-generation. In the presence of beta-lactamase enzymes cefixime is highly stable. Many organisms which are resistant to penicillins and to cephalosporin because of the presence of beta-lactamases, could be susceptible to cefixime. Cefixime inhibits the mucopeptide synthesis in the bacterial cell all this gives cefixime it's antibacterial activity. Cefixime is used to treat bacterial infections of the lungs, throat, urinary tract, ears. belongs to cephalosporin antibiotics group, which stop the growth. Cefixime is available in the tablet capsule, chewable tablet, and oral (by mouth) suspension forms and is taken once or twice daily, with or without food.The absolute bioavailability of cefixime under fasting or fed conditions is approximately 40-50%, however, time to maximal absorption is increased approximately 0.8 hours when administered with food. It is absorbed from entire GI tract.[8]

MATERIALS AND METHODS

Cefixime was a gift sample from Alkem Laboratories Pvt. Ltd., India. Microcrystalline Cellulose were purchased from Lobachem Pvt. Ltd (Mumbai). Mimosa pudica seed mucilage were purchased from akhand aushadhi bhandar (indore), PVP K30 were purchased from Lobachem Pvt. Ltd. Magnesium stearate were purchased from Lobachem Pvt. Ltd. Talc were purchased from Lobachem Pvt. Ltd.

Identification of pure drugs

Identification of drug

Ultraviolet spectroscopy

Preparation of standard stock solution

A standard stock solution of cefixime was prepared by dissolving accurately weighed 50 mg of cefixime in methanol in a 50 ml volumetric flask and the volume was made up to 50 ml with methanol to obtain a stock solution of 1000 µg/ml. (stock solution first)

Determination of wavelength

After that 10µg/ml was prepared by 1000 µg/ml stock solution. The resulting solution was scanned between 200 and 400 nm by UV spectrophotometry. The λmax was found to be 285 nm λ max and 285 nm was considered as analytical wavelength.

Preparation of calibration curve in 0.1N HCl solution

- Accurately weighed quantity of cefixime 50 mg was dissolved in a methanol in a 50 ml volumetric flask and the volume was made up to 50 ml with methanol to obtain a stock solution of 1000 µg/ml(stock solution first).
- From the standard stock solution, After that 10µg/ml was prepared by 1000 µg/ml stock solution. 1 ml was pipetted into 10 ml volumetric flask. The volume was made upto 10 ml with 0.1 NHCl. The resulting solution contains 100µg/ml.(stock solution second)

Preparation of calibration curve

From the above solution 0.2, 0.4, 0.6, 0.8 and 1ml pipetted out and diluted to 10 ml with 0.1N HCl and the resulting solution containing 10µg/ml.

Preparation of calibration curve of cefixime in phosphate buffer solution (pH 6.8)

Preparation of pH 6.8 phosphate buffer

Placed 50.0 ml of 0.2M potassium dihydrogen phosphate in a 200 ml volumetric flask. Added the 22.4 ml of 0.2M sodium hydroxide and then added water to volume.

- A standard stock solution of cefixime was prepared by dissolving accurately weighed 100mg of cefixime in pH 6.8 phosphate buffer solution 100 ml volumetric flask. The volume was made up to 100 ml with phosphate buffer solution, pH 6.8 to obtain a stock solution of 1000µg/ml (stock solution first).
- From the standard stock solution, 1 ml was pipetted into 10 ml volumetric flask. The volume was made up to 10 ml with 6.8 pH phosphate buffer. The resulting solution contains 100µg/ml (stock solution second).

Preparation of Calibration curve

From the above solution 0.2, 0.4, 0.6, 0.8 and 1 ml was pipetted out and diluted to 10 ml with phosphate buffer to give the final concentration of 2,4,6,8 and 10µg/ml. Respectively and take the absorbance at lambda max against distilled water as the blank plotted the calibration curve.

Determination of solubility of cefixime

Saturation shake-flask method: Sufficient amount of cefixime was added to 5 ml glass vials containing distilled water, phosphate buffer (pH 6.8) and 0.1 N HCl (pH 1.2). The vials were shaken mechanically for 12h on mechanical shaker at 37 ±2°C. The solutions were allowed to equilibrate for next 24 h. The solution was transferred into tubes and centrifuged for 5 min at 2,000rpm.The supernatants of each vial were filtered by membrane filter and after appropriate dilutions it was analyzed by UV visible spectrophotometer at 285 nm for drug content. The study was performed in triplicate.[9-11]

Extraction of mucilage from mimosa pudica seed

M. pudica seeds were soaked in sufficient quantity of water for 10 h; the hydrated mucilage along with seeds was spread in a thin layer on the stainless steel tray and dried in an oven at 50°C for 4–5 h. The dried mucilage was scraped from the tray by blade and separated from the seeds by passing through no. 18 mesh. The mucilage was further purified by winnowing to separate seed husk.[12-14]

Preformulation study

Characterization of mimosa pudica seed mucilage

- **Extraction yield:** The percentage yield was calculated as the percentage of the amount of dry mimosa pudica seed sample used before the extraction process and the amount of powder of mucilage obtained after the extraction.[15-25]

  Percentage yield = weight of dried mucilage obtained / weight of seed used ×100

- **Swelling index (SI)**: Swelling index is the volume taken up by the swelling of Mimosa pudica seed mucilage under specified conditions. It was determined by weighing 500 mg of mucilage, and introducing the mucilage into a 25 ml measuring cylinder and 12.5 ml of water was added and the mixture was shaken thoroughly in every 10 min for 1 hour. It was then allowed to stand for 3 hours at room temperature. Then the volume occupied by

mucilage was measured. The same procedure was repeated thrice and the mean value was calculated.

Volume of swollen mucilage-volume of dried mucilage / volume of dried mucilage×100

- **Bulk density:** An accurately weighed quantity of the powder was carefully poured into the graduated measuring cylinder and the volume was measured. The bulk density of the powder is denoted by gram per ml. It was calculated using the formula.

  Bulk density = Weight of powder (in gm)/volume packed (in ml)

- **Tapped density:** The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume occupied in the cylinder and the weight of the tapped mucilage was measured. The tapped density was calculated using the formula:

  Tapped density = Weight of powder in gm/tapped volume in ml

- **Hausner's ratio:** It is the number that is related to the flow ability of powder or granules.

  Hausner's ratio = Tapped density /bulk density

- **Carr's compressibility index:** It is an indication of the compressibility of a granule or powder. It denote flow ability of granule

  Carr's index (%) =Tapped density - Bulk density ×100

- **Angle of repose:** A funnel was fixed with the help of tripod stained and secured its tip at a height (h) of 2cm above graph paper was placed on a horizontal surface. The powder was dropped and the radius (r) was measured.[25]

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

Drug excipient interaction study

Drug excipient interaction study of cefixime: The mixtures of drugs and excipient were prepared in 1:1 ratio by triturating and then passed through sieve # 30. Samples of drug and excipient were placed in vial, closed and labelled. Then the vials were stored under conditions at 40 ºC and at 75 % RH in humidity chamber. Physical and chemical change of all the mixtures were done on 0^{th} day and 15^{th} day by TLC.[27,29]

Thin layer chromatography: The stationary phase were prepared by silica gel G. The mixture of organic solvent methanol: water: acetic acid (7:2:1 v/v/v) was used as mobile phase.

Calculation of Rf value: Rf value calculate by following formula

Retention factor: distance travel by solute ÷ distance travel by solvent.

SELECTION OF EXCIPIENT

Selection of excipient for sustained release tablet

Table No. 1 List of excipient for sustained release tablet.

S. No.	Name of Excipient	Purpose
1.	Mimosa pudica seed mucilage	Release retardant
2.	Microcrystalline cellulose	Disintegrant agent
3.	PVP K30	Binder
4.	Magnesium stearate	Lubricant
5.	Talc	Glidant

Formulation

Table No. 2 Formulation.

S. No.	Name	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1.	Cefixime	400	400	400	400	400	400	400	400	400
2.	Mimosa pudica seed mucilage	100	100	100	150	150	150	200	200	200
3.	Microcrystalline cellulose	100	110	120	100	110	120	100	110	120
4.	PVP K30	1%	1%	1%	1%	1%	1%	1%	1%	1%
5.	Magnesium stearate	5	5	5	5	5	5	5	5	5
6.	Talc	5	5	5	5	5	5	5	5	5

Preparation of granules

Sustained release tablet of cefixime was prepared by wet granulation technique as follows:[30]

Shifting→ Dry mixing→ Granulation→ Drying →Lubrication

Wet granulation process

Wet granulation is the most widely used process of agglomeration. It involves wet massing of the powder blend with a binding liquid, wet sizing and drying.

Important steps involved in the wet granulation

1. The drug and excipient were mixed
2. Binder solution was prepared
3. The binder solution was mixed with powder mixture to form wet mass screens.
4. Wet mass was course screened using a sieve no.40.
5. Moist granules were dried in oven at 50^{o}C for 1 hrs.

6. The dry granules were screened through a sieve no.40.
7. Screened granules were Mixed with disintegrant, glidant, and lubricant.[30]

Evaluation of granules Evaluations of Granules Properties

The flow properties of granules were characterized in terms of angle of repose, Carr index and Hausner's ratio. The bulk density and tapped density were determined and from this data Carr's index and Hausner's ratio were calculated

Post compression parameter

- **Compression:** The tablet compression granules were compressed in rotary tablet compression machine using 12mm deep concave punches plan on both side at required pressure.
- **Drug content:** 10 tablets was weighed and powdered. Weight accurately a quantity of the powder containing about 0.1 gm cefixime and it was transferred into a 100 ml volumetric flask. Add 6.8 phosphate buffer up to the mark. After few minutes the solution was filtered, and diluted 1 ml of filtrate to 10 ml of 6.8 phosphate buffer. Further diluted 1 ml of above solution to 10ml of 6.8 phosphate buffer and measured absorbance of resulting solution at lambda max and the drug content was calculated.[31-32]
- **In vitro Drug release:**

  In-vitro drug release studies details

Table No. 3: In-vitro drug release studies details.

Apparatus used	USP type II dissolution test apparatus
Dissolution medium	0.1 M HCl, 6.8 pH phosphate buffer solution.
Dissolution medium volume	900 ml
Temperature	37±0.5 C°
Speed of basket paddle	100 rpm
Sampling intervals	60 min
Amt. of sample withdrawn	5 ml
Absorbance measured	285 nm

- In vitro drug release studies were carried out using A USP type II dissolution apparatus (paddle method) was used for the studies. The dissolution media was 0.1 M HCl solution for first 2 hr followed by pH 6.8 phosphate buffer solution for 12 hrs. At specified time intervals, 5 ml samples were withdrawn and replaced with the same volume of fresh dissolution medium maintained temperature. The withdrawn samples were rapidly filtered using a whatman filter paper and diluted appropriately with the dissolution medium. The

diluted filtrates were analyzed by UV spectrophotometry at 285 nm. The amount of cefixime matrix tablets was determined using regression data obtained from a calibration plot of cefixime in 0.1 N HCl solution and phosphate buffer pH 6.8. From these, plots of percentage drug released from the tablet formulations versus time were established.[33-35]

- **Thickness:** Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and the thickness of the tablets was calculated by the use of verniercalliper. The tablets exhibited uniform thickness among the different formulations**.** **[36-37]**
- **Weight variation test:** randomly selected 20 tablets from each formulation and weighed individually to check for weight variation. The following percentage deviation in weight variation is allowed in Indian Pharmacopoeia.

  Percentage weight variation= Individual weight- average weight/average weight×100
- **Friability:** The roche friabilator was used to determine friability of tablets. Friabilator expressed the percentage surface erosion (%). Ten tablet weighed and transferred into friabilator. The friabilator was rotated at 25 rpm for 4 minutes or run up to 100revolutions. The tablets were weighed again. A maximum loss of weight not greater than 1.0 % is acceptable for most tablets**.** The % friability was calculated [33,35]

  Percentage friability = Weight before test - weight after test / weight after test × 100
- **Hardness:** Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^3. Three tablets were randomly picked and hardness of the same tablets was determined by placed in contact with lower plunger and a zero reading was taken. Then the force was applied by the plunger against a spring by tightening the screw until the tablet fractured. Then the value was noted from scale at which tablet crushed.
- **Swelling Index**: The swelling behavior of cefixime tablets was determined at 37 ± 0.5°C in phosphate buffer pH 6.8, over 6 h. Formulations were individually kept in a petridish containing 50 ml of the buffer solution. At the end of the specific period the tablet was removed, blotted with a tissue paper and weighed. The extent of swelling was calculated.[33]

Swelling index = Weight after swelling - weight before swelling /weight before swelling×100

RESULT AND DISCUSSION

Mimosa pudica seed mucilage: Mucilage from mimosa seed was extracted according to procedure and various studies was done and results are as follows.

Table No. 4: Mucilage characteristics.

S.No.	Parameters	Results(Mean ± SD)
1	Extraction yield	80±1.5
2	Swelling Index	11.6±0.86
3	pH of mucilage	7.52±0.05
4	Bulk density	0.256±0.005
5	Tapped density	0.396±0.013
6	Carr's index	35.38±1.09
7	Hausner's ratio	1.543±0.02
8	Angle of repose	28.40±0.080

PREFORMULATION

Drug characterization

Determination of wavelength using UV spectrophotometric analysis

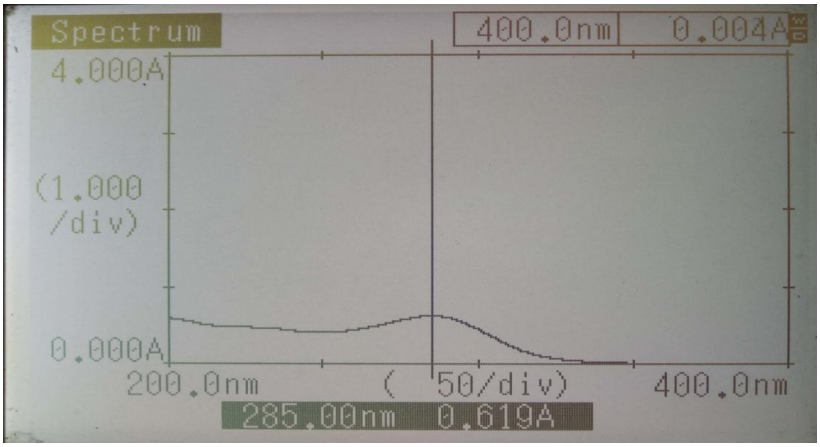

Figure 1: λ max of cefixime.

The maximum wavelength of cefixime was found at 285 nm.

Preparation of calibration curve

The calibration curve of cefixime: The calibration curve of cefixime in 0.1 N HCl and distilled water and buffers (6.8 pH phosphate buffer) was prepared and shown below.

Absorbance data of cefixime in water for preparation of calibration curve at 285 nm

Table No. 5: Absorbance data of cefixime in water.

S. No.	Concentration (µg/ml)	Absorbance (mean ± standard deviation)
1.	2	0.141 ± 0.006
2.	4	0.196 ±0.003
3.	6	0.249 ± 0.005
4.	8	0.304 ±0.006
5.	10	0.361 ±0.001

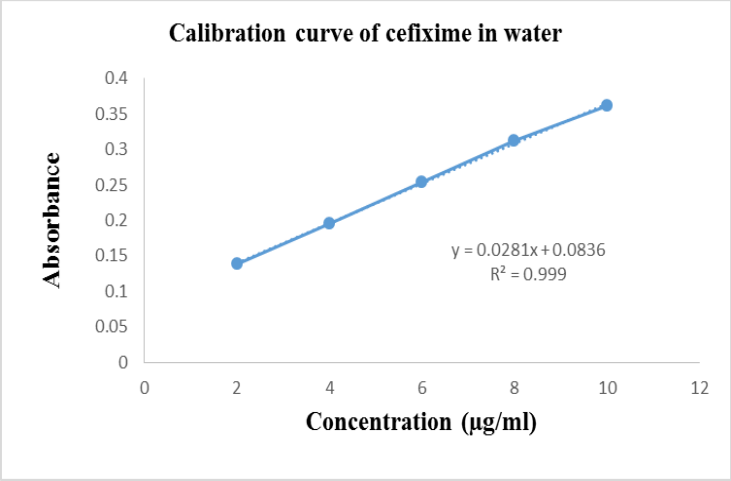

Figure 2 Calibration curve of cefixime in water at 285 nm.

Absorbance data of cefixime in water at 285 nm follows Lambert-Beer's law in the range of 2µg/ml to 10µg/ml.

Absorbance data of cefixime in 0.1 N HCL solution for preparation of calibration curve at 285nm

Table No. 6: Absorbance data of cefixime in 0.1 N HCL solution.

S. No.	Concentration (µg/ml)	Absorbance (Mean ± Standard deviation)
1.	2	0.146 ± 0.002
2.	4	0.167 ± 0.001
3.	6	0.189 ± 0.002
4.	8	0.213 ± 0.006
5.	10	0.233 ± 0.008

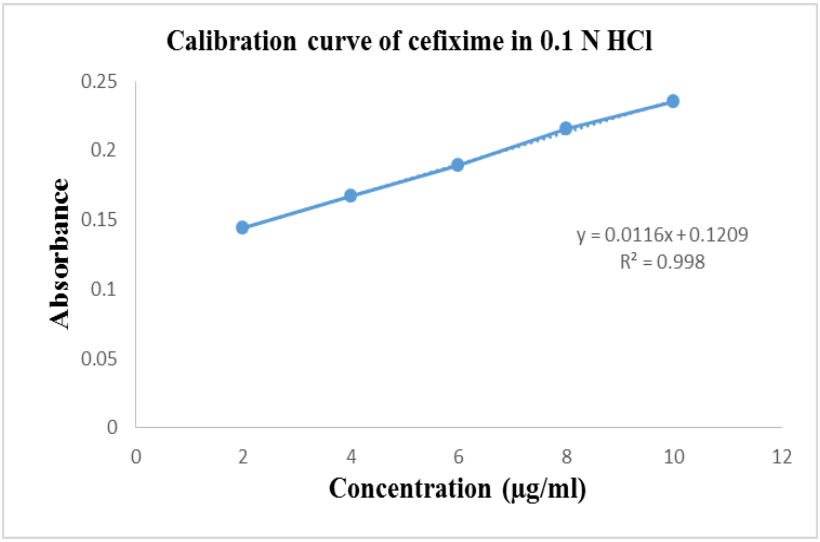

Figure 3: Calibration curve of cefixime in 0.1 N HCL solution at 285 nm.

Absorbance data of cefixime in 0.1 N HCL solution at 285 nm follows Lambert-Beer's law in the range of 2µg/ml to 10 µg/ml.

Absorbance data of cefixime in 6.8 pH buffer for preparation of calibration curve at 285 nm

Table No. 7: Absorbance data of cefixime in 6.8 pH buffer.

S. No.	Concentration (µg/ml)	Absorbance (Mean± Standard deviation)
1.	2	0.126±0.012
2.	4	0.364±0.008
3.	6	0.471±0.009
4.	8	0.602±0.009
5.	10	0.769±0.009

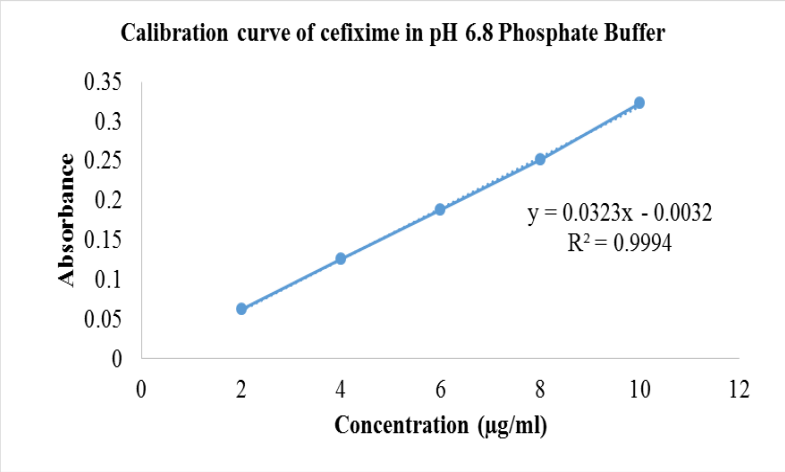

Figure 4 Calibration curve of cefixime in 6.8 pH buffer at 285 nm.

Absorbance data of cefixime in 6.8 pH buffer solution at 285 nm follows Lambert-Beer's law in the range of 2µg/ml to 10µg/ml.

Determination of solubility

Solubility of drugs in various solution and buffer: The solubility of cefixime in various solution and buffer were studied and the result of study shown below

Table No. 8: Solubility of drugs.

S. No.	Solvent	Solubility of drug (mg/ml) (Mean ± SD)
1.	0.1 N HCl solution	4.51±0.05
2.	Water	2.37 ± 0.13
3.	6.8 pH buffer	139.37 ± 2.16

Drug Excipient interaction study

The drug was found to be compatible with various excipient which were selected for formulation of sustained release tablet the compatibility was assessed by TLC (thin layer chromatography) and the retention factor of all ratios found similar.

Table No. 9: List of Drug Excipient Retention Factor.

S. No.	Drug Excipient Ratio (1:1)	Initial appearance Present day	Final appearance After 15 days	Retention factor Present day	Retention factor After 15 days
1.	Cefixime	Yellow Crystalline Powder	No change	0.91	0.92
2.	Cefixime: Mucilage	Brown Powder	No change	0.96	0.95
3.	Cefixime: MCC	Whitish yellow mixture	No change	0.95	0.98
4.	Cefixime:PVPK30	Whitish yellow mixture	No change	0.93	0.94
5.	Cefixime: Magnesium stearate	White mixture	No change	0.96	0.96
6.	Cefixime: Talc	Whitish yellow mixture	No change	0.95	0.96
7.	Cefixime: All excipient	Brownish white powder	No change	0.96	0.95

Formulation and optimization

Table No. 10: Formulation and Optimization of sustained release tablet.

S. No.	Name	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1.	Cefixime	400	400	400	400	400	400	400	400	400
2.	Mimosa pudica seed mucilage	100	100	100	150	150	150	200	200	200
3.	Microcrystalline cellulose	100	110	120	100	110	120	100	110	120
4.	PVP K30	1%	1%	1%	1%	1%	1%	1%	1%	1%
5.	Magnesium stearate	5	5	5	5	5	5	5	5	5
6.	Talc	5	5	5	5	5	5	5	5	5

Precompression parameter: Result of precompression parameter of cefixime granules.

Table No. 11: Results of Precompression Parameter of cefixime granules.

S. No.	Formulation	Bulk density (gm/cm^3) (Mean ± SD)	Tapped density (gm/cm^3) (Mean ± SD)	Carr's index %(Mean ± SD)	Hausner's ratio (Mean ± SD)	Angle of repose (^{0}) (Mean ± SD)
1.	F1	0.386 ± 0.01	0.453 ± 0.02	14.67 ± 0.63	1.17 ± 0.008	15.3^0± 0.06
2.	F2	0.349 ± 0.01	0.402 ± 0.017	12.99 ± 0.60	1.14± 0.01	16.82^0± 0.24
3.	F3	0.331 ± 0.01	0.406± 0.016	18.44 ± 0.53	1.22 ± 0.01	15.51^0± 0.21
4.	F4	0.329 ± 0.01	0.399± 0.015	17.35 ± 0.49	1.20 ± 0.01	23.47^0± 0.27
5.	F5	0.320± 0.01	0.383 ± 0.01	16.48 ± 0.59	1.19 ± 0.01	22.78^0± 0.08
6.	F6	0.317 ± 0.009	0.378 ± 0.014	16.01 ± 0.59	1.19 ± 0.01	27.60^0± 0.2
7.	F7	0.316 ± 0.009	0.372 ± 0.01	15.1 ± 0.53	1.17 ± 0.02	25.58^0± 0.08
8.	F8	0.305 ± 0.008	0.357 ± 0.012	14.55 ± 0.46	1.16 ± 0.03	30.85^0± 0.9
9.	F9	0.295 ± 0.008	0.343 ± 0.01	13.86± 0.39	1.30 ± 0.01	31.49^0± 0.16

Post compression parameter

In vitro drug release of tablets: Cumulative drug releases of cefixime sustained release tablet are as follows

TableNo.12 Cumulative % drug release of cefixime sustained release tablet.

S. No.	Time (Hrs)	% Cumulative drug release								
		F1 (Mean±SD)	F2 (Mean±SD)	F3 (Mean±SD)	F4 (Mean±SD)	F5 (Mean±SD)	F6 (Mean±SD)	F7 (Mean±SD)	F8 (Mean±SD)	F9 (Mean±SD)
1	1	15.26 ±0.07	27.84 ±0.1	24.95 ±0.2	28.50 ±0.1	17.74 ±0.1	18.51±0.1	22.55±0.1	31.17 ±0.08	31.24 ±0.1
2	2	28.38 ±0.07	41.44 ±0.2	34.63 ±0.3	37.27 ±0.2	24.84 ±0.1	25.57±0.1	30.28±0.07	40.44 ±0.1	40.89 ±0.1
3	3	42.76 ±0.6	52.68 ±0.1	41.75 ±0.3	42.44 ±0.1	31.70 ±0.1	32.70±0.2	41.63±0.3	47.41 ±0.1	53.54 ±0.1
4	4	62.28 ±0.1	63.96 ±0.1	49.33 ±0.09	55.36 ±0.1	42.52 ±0.2	41.50±0.1	55.49±0.4	53.74 ±0.07	59.24 ±0.1
5	5	68.60 ±0.07	69.16 ±0.1	55.07 ±0.1	60.67 ±0.2	53.36 ±0.1	48.17±0.1	68.94±0.2	60.47 ±0.2	69.09 ±0.1
6	6	73.38 ±0.08	78 ±0.06	68.68 ±0.3	69.9 ±0.07	61.49 ±0.2	53.30±0.1	73.15±0.4	70.34 ±0.06	70.47 ±0.04
7	7	81.82 ±0.06	80.76 ±0.08	78.13.±0.04	70.48 ±0.04	69.38 ±0.2	69.11 ±0.08	78.39±0.7	84.54 ±0.04	79.50 ±0.1
9	8	90.21 ±0.06	87.02 ±0.07	85.09 ±0.1	81.68 ±0.04	82.90 ±0.04	84.35 ±0.7	81.59 ±0.04	85.53 ±0.04	86.55 ±0.07
10	12	93.57 ±0.04	92.83 ±0.06	94.91 ±0.08	96.98 ±0.04	98.51 ±0.06	95.22 ±0.6	95.61 ±0.08	93.55 ±0.04	95.88 ±0.08

From the study it was found that F5 is best from all formulations which were used to formulate sustained release tablet.

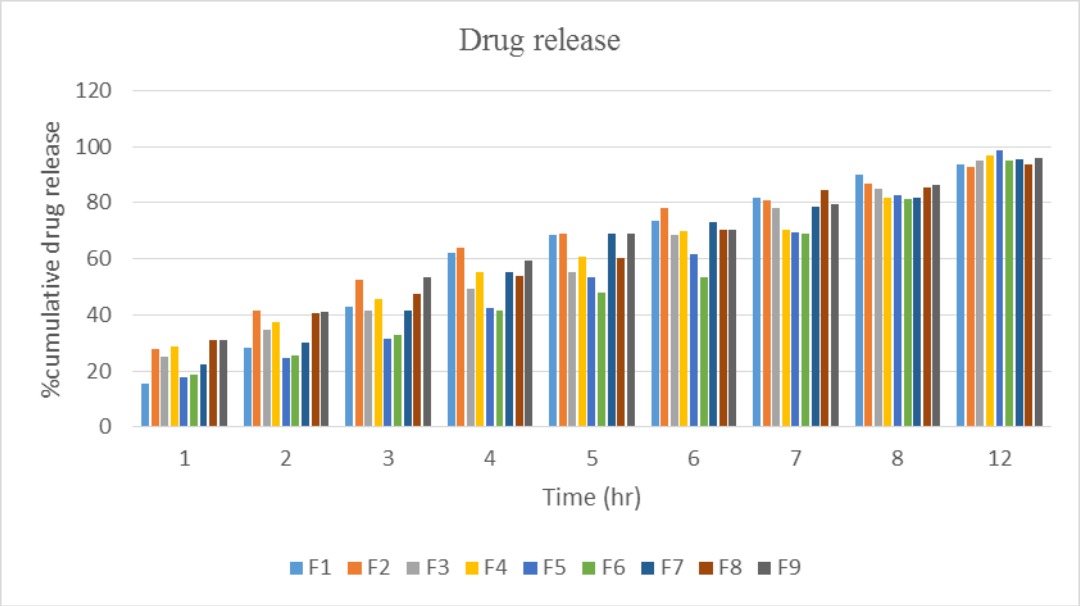

Figure: 5 Cumulative % drug release of cefixime sustained release tablet.

Evaluation of sustained release tablet

Pre compression parameter: Result of pre compression parameters of optimized layers of sustained release tablets were as follows

Table No. 13: Precompression parameter of optimized batch F5.

S. No.	Drug	Bulk Density (gm/cm^3) (Mean ± SD)	Tapped Density (gm/cm^3) (Mean ± SD)	Carr's Index % (Mean± SD)	Hausner's Ratio (Mean ± SD)	Angle of Repose (Mean ± SD)
1.	Cefixime	0.320± 0.01	0.45±0.01	17.43±2.6	1.18±0.01	21.66±0.05

Post compression Parameter: Result of optimized sustained release tablets were as follows

Table No. 14: Post compression Parameter.

S.No.	Thickness (Mean ± SD)	Hardness (Mean ± SD)	Weight variation(Mean ± SD)	Friability (Mean ± SD)	Drug content (Mean ± SD)
1.	4.7±0.05	5.33±0.2	670±4.47	4.14±0.9	96.25±0.8

Swelling index of sustained release tablet

Table No. 15: Swelling index of sustained release table.

S. No.	Time (hour)	Swelling Index % (Mean ± SD)
1.	1	2.48±0.5
2.	2	9.94±0.5
3.	3	18.90±0.8
4.	4	27.36±0.8
5.	5	33.32±0.8
6.	6	40.79±0.8

In-vitro drug release of sustained release tablet: Drug release was determine according to procedure of I.P. and results shown below in table:

Table No.16: % cumulative drug release.

S.No.	Time (hrs)	% Cumulative drug release of sustained release tablet
		Cefixime
1.	1	17.74±0.1
2.	2	24.84±0.1
3.	3	31.70±0.1
4.	4	42.52±0.2
5.	5	53.36±0.1
6.	6	61.49±0.2
7.	7	69.38±0.2
8.	8	82.90±0.04
9.	12	98.51±0.06

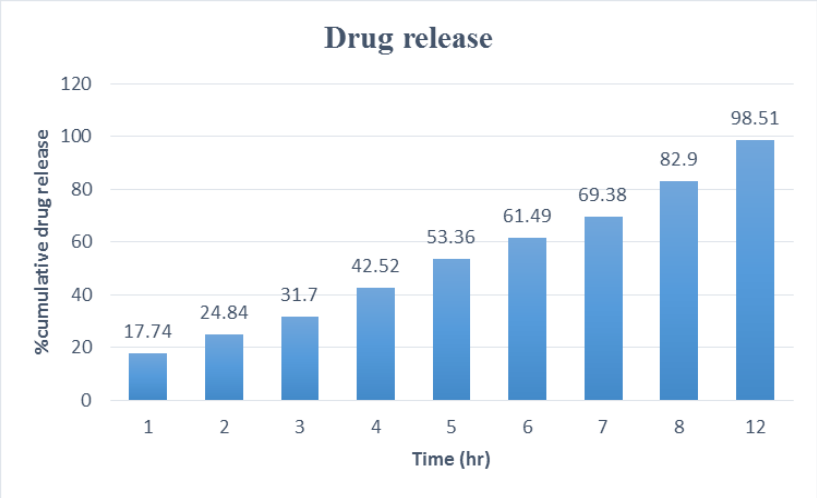

Figure: 6 Cumulative % drug release of cefixime sustained release tablet.

CONCLUSION

Conventional dosage forms are prompt release in nature for the treatment of chronic diseases. To maintain drug concentration of conventional dosage forms within the therapeutic range, it is necessary to take dosage several times a day, which results in fluctuation of drug levels in body. To reduce frequency of dosage form several techniques have been developed. The sustain release techniques are capable of controlling the rate of drug release and sustaining the duration of therapeutic activity and targeting the drug to specific site. Sustained release dosage form improves the patient compliance and also decreases adverse drug reaction. Sustained release dosage form maintains therapeutic concentration of drug in blood. For formulation of sustained release tablet, release retardant agents are used which sustain the duration of therapeutic activity.

Objective was to prepare sustained release tablet of cefixime using mimosa pudica seed mucilage. The aim of present study was to develop extended release formulation of cefixime for treatment of UTI infection. In present study mimosa pudica seed mucilage played major role in sustained release dosage form. It was retarding the release of tablet. The mimosa pudica seed has diuretic activity which played an important role in the treatment of UTI infection.

In present work release retardant mucilage were isolated from mimosa pudica seed and characterized. The physical property like bulk density, tapped density, Hausner's ratio, Carr's index, angle of repose were determined.

In present work procured cefixime was characterized by various method. The λmax of cefixime was determined by UV- visible spectroscopy and was found to be 285 nm. In preformulation study calibration curve of cefixime were prepared in various solvent (water, pH 6.8 phosphate buffer and 0.1 N HCL). The solubility of cefixime in distilled water, 0.1 N HCL, pH 6.8 phosphate buffer, 0.1 N HCL was determined by UV visible spectroscopy. The drug excipient interaction study was performed at 40 ºC for 15 days and estimated by TLC, all excipient of formulation were found to be compatible with drug similar Rf value.

Optimized formulation was found by preparing all optimized formulations with same amount of cefixime 400 mg and different amounts of mucilage and MCC. Prepared tablets were evaluated for physical and chemical properties. For sustained release tablets in vitro study was carried out in 0.1 N HCL for first 2 hours followed by pH 6.8phosphate buffer up to 12 hours using USP type II apparatus at 100 rpm. To study the effect of pH of medium and in vitro release, release studies were carried using pH change method and in phosphate buffer pH 6.8.

Formulation F5 was showing the highest drug release so this formulation was selected for further study. Drug release of optimized F5 batch was found 98.51% which was found within 12 hours. In order to formulate sustained release tablet, cefixime was mixed with mucilage and other excipient and the PVP solution was added to form wet mass which than passed through the sieve no. 16 to form granule. These formed granules were subjected to various characterizations like Bulk density, Tapped density, Carr's index, Hausner's ratio and angle of repose to determine its flow characteristics.

Drug content in formulation F5 were found to be 98.51% and which sustained the release of drug for 12 hours. Hence it can be concluded that this formulation can be employed to retard the release of drug.

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