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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF DISPERSABLE TABLET OF CEFIXIME TRIHYDRATE

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Abstract:

The objective of the study is to develop cefixime trihydrate orally dispersible tablet using co processed super disintegrants and comparative study with the marketed product. Cefixime trihydrate orally dispersible tablet was prepared by direct compression method using co processed super disintegrants such as cross povidone and sodium starch glycolate in different concentrations. The developed oral disintegrating tablets were evaluated for different physical chemical evaluations like drug content, hardness, friability, weight variation, wetting time, In vitro disintegration time, *In-vitro* drug release etc. All formulations had shown the results within the prescribed limits.

Keywords: Cefixime trihydrate, Dispersible tablet, Direct compression, co processed superdisintegrants, Release kinetics

Introduction

Oral mucosal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both injectable and enteral methods. Because the oral mucosa is highly vascularized, drugs that are absorbed through the oral mucosa directly enter the systemic circulation, by passing the gastrointestinal tract and first-pas smetabolism in the liver. For some drugs, this results in rapid onset of action via a more comfortable and convenient delivery route than the intravenous route. Not all drugs, however, can be administered through the oral mucosa because of the characteristics of the oral mucosa and the physicochemical properties of the drug.

The oral route of administration is considered as the most widely accepted route. The unique environment of the oral cavity offers its potential as a site for drug delivery. Because rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver.

The continuous secretion of saliva results in rapid removal of released drug and this may desire that the oral cavity be restricted to the delivery of drugs, which have a short systemic circulation.

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphasia patients turned the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenterals are painful drug delivery, so most patient incompliance.[1,2,3]

Dispersible tablets are uncoated or film-coated tablets that can be dispersed in liquid before administration giving a homogenous dispersion. Dispersible tablets usually disintegrate within three minutes when put in water or a small amount of breast milk.[4]

Cefixime trihdrate is third generation cephalosporin, mainly used in treatment of respiratory, urinary, skin and soft tissue infection caused by gram positive and gram negative bacteria. Cefixime trihydrate is available in oral tablet and oral suspension forms in the market. Cefixime trihydrate is molecule which has a very low solubility in water. Therefore oral bioavailability of the tablet form is 50% less than cefixime trihydrate given intravenously. Tablets which contain 100mg and 200mg of cefixime trihydrate are available in market. Cefixime trihydrate is hydrophobic in nature and has a water contact angle greater than 90^0. Hence, cefixime trihydrate has a low solubility and poor disintegration in water when used in a formulation. In the prior art, several methods have been developed in order to solve the solubility problem of cefixime trihydrate in water and increase the disintegration rate and thus absorption of it. [5]The aim of present work to develop a dispersible dosage form which upon dispersion in water forms a homogenous dispersion with reduced sedimentation rate, thus ensuring uniformity of dosage.

MATERIALS AND METHODS

Cefixime trihydrate was obtained as a Gift sample from Dr. Reddy's Laboratories Limited, Hyderabad, Crospovidone, Sodium starch glycolate, Micro crystalline cellulose was obtained from S.D fine chemicals limited, Mumbai. All other chemicals and reagents used were of analytical grade.

Preformulation Studies

Preformulation testing is the first step in the rationale development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. Weighed amount of drug (3mg) was mixed with 100mg of potassium bromide (dried at 40-50°C). The mixture was taken and compressed under 10-tonpressure in a hydraulic press to form a transparent pellet. The pellet was scanned by IR spectrophotometer. Similar procedure is followed for all relevant excipients used.

Preparation of dispersible tablets of Cefixime trihydrate

Cefixime Trihydrate dispersible tablets were prepared by direct compression method by using co-processed super disintegrants like Crospovidone, Sodium Starch Glycolate. Mannitol, Microcrystalline Cellulose as a diluent, Sodium saccharin as a sweetening agent, Mint as a flavor, Magnesium Stearate, Talc used as a lubricant and glidant. All the ingredients (except granular directly compressible excipients) were passed through # 60-mesh separately. Then the ingredients were weighed and mixed in geometrical order after sufficient mixing of drug as well as other components and compressed into tablets of 150mg using 8mm round flat punches on 12 station rotary tablet machine. The formulations are shown Table 1.

Evaluation of blended characteristics of cefixime trihydrate

Evaluation of Granules[6,7,8,9]

Determination of angle of repose

Angle of repose is an indication of the frictional forces excited between granule particles. It is the maximum angle possible between the surface of the pile of granules and the horizontal plane:

$$\mathbf{Tan\ \theta = h/r}$$

Where, θ = the angle of repose
h = height of the heap of the powder
r = radius of the heap of the powder

Determination of Bulk Density:

It is the ratio of total mass of powder to the bulk of powder. It is measured by pouring the weighed powder into a measuring cylinder and the volume was noted.
It is expressed in g/cm^3 and is given by

$$\text{Bulk Density} = \frac{\text{Mass of powder}}{\text{Bulk volume of the powder}}$$

Tapped Density:

It is the ratio of total mass of powder to the tapped volume of powder. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/cm^3 and is given by

$$\text{Tapped Density} = \frac{\text{Mass of powder}}{\text{Tapped volume of the powder}}$$

Hausner's Ratio:

It indicates the flow properties of the granules and is measured by the ratio of tapped density to the bulk density.

Hausner's Ratio = Tapped density/Bulk density

Compressibility index (Carr's Index):

It helps in measuring the force required to break the friction between the particles and the hopper. It is expressed in % and given by

$$CI = \frac{(\text{Tapped Density} - \text{Bulk Density}) \times 100}{\text{Tapped Density}}$$

Compressibility index is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. A material having values of less than 20% has good flow property.

Evaluation of post-compression parameters [6,7,10,11,12]

Weight variation

The weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. The IP weight variation test is done by 20 tablets were selected randomly from each formulation after compression, weighed individually using a "Electronic weighing balance" and average weight was determined. The individual weights are compared with the average weight for the weight variation. The tablets met the IP specification that not more than 2 tablets are outside the percentage limits and no tablet differs by more than 2times the percentage limit.

Tablet hardness

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of each batch of tablet was checked by using "Monsanto hardness tester". The hardness was measured in terms of kg/cm^2. 5 tablets were chosen randomly and tested for hardness. The average hardness of 5 determinations was recorded.

Friability

Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients.

Tablet thickness

Thickness of the tablet is important for uniformity of tablet size. Thickness was measured using "Vernier Callipers". It was determined by checking the thickness of ten tablets of each formulation.

Drug content uniformity

The tablets were tested for their drug content uniformity. At randomly selected 5 tablets from each formulation were finely powdered and powder equivalent to 100 mg of Cefixime trihydrate drug was weighed accurately and dissolved in 100ml of phosphate buffer solution at p^H 7.2. The solution was shaken thoroughly. The un-dissolved matter was removed by filtration through Whatman No.41 filter paper. Then the serial dilutions were carried out. The absorbance of the diluted solutions was measured at 288nm. The concentration of the drug was computed from the standard curve of the Cefixime trihydrate in phosphate buffer solution at p^H 7.2.

***In-vitro* Disintegration time**

Tablet disintegration is an important step in drug absorption. The test for disintegration was carried out in "Electro lab USP disintegration test apparatus". It consists of 6 glass tubes which are 3 inches long, open at the top, and held against a 10 mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tablets, one tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker containing phosphate buffer p^H 7.2 as medium. The volume of medium was 900ml and temp was 37°C ± 0.2°C. The time taken for the complete disintegration of the tablets with no palatable mass remaining in the apparatus was measured.

***In-vitro* Dissolution studies**

Dissolution testing of dispersible tablet of cefixime trihydrate was carried out with "Paddle type-II USP dissolution test apparatus" at rpm 50 and temperature 37±0.5°C both dissolution media and water. At each specified intervals of time 5 ml sample was withdrawn and replaced by fresh media. The samples were analytically tested to determine the concentration by UV spectroscopy method at wavelength of 288 nm. The % drug release was calculated using an equation obtained from the calibration curve.

Mathematical modeling of drug release profile[11]

The cumulative amount Cefixime trihydrate release from the formulated tablets at different time intervals were fitted to zero order kinetics, first order kinetics, higuchi model and korsmeyer-peppas model to characterize mechanism of drug release.

Zero Order Kinetics

It describes the system in which the release rate is independent of its concentration.

$$Qt = Q_0 + K_0t$$

Where, Qt = amount of drug dissolved in time t
Q_0 = initial amount of drug in the solution
K_0 = zero order release constant

If the zero order drug release kinetic is obeyed, a plot of $Q_t$versus t will give straight line with a slope of K_0 and an intercept at Q_0.

First Order Kinetics:

It describes the drug release from the system in which the release rate is concentration dependent.

$$\log Qt = \log Q_0 + K_1t/2.303$$

Where, Qt = amount of drug dissolved in time
Q_0 = initial amount of drug in the solution
K_1 = first order release constant
If the release pattern of drug follows first order

kinetics, then a plot of log (Q_0 - Q_t) versus t will be straight line with a slope of $K_1/2.303$ and an intercept at t= 0 of $\log Q_0$.

Higuchi Model:

It describes the fraction of drug release from a matrix is proportional to square root of time.

$$Mt/M\infty = K_H\, t^{1/2}$$

Where,

Mt and M∞ are cumulative amount of drug release at time t and infinite time,

K_H = Higuchi dissolution constant reflection formulation characteristics.

If the Higuchi model of drug release is obeyed, then a plot of Mt/M∞ versus $t^{1/2}$ will be straight line with slope of K_H.

Korsmeyer- Peppas Model:

The power law describes the fractional drug release is exponentially related to the release time and adequately describes the release of drug from slabs, cylinders and spheres, as expressed in following equation:

$$Mt / M\infty = Kt^n$$
$$\text{Log } (Mt / M\infty) = \log K + n \log t$$

Stability Studies[36]

Stability can be defined as the capacity of drug product to remain within specifications established to ensure its identity, strength, quality, and purity. The optimized formulation was subjected for stability study. The selected formulations were packed in aluminum foil in tightly closed container. They were then stored at 40ºC / 75% RH and evaluated for their physical appearance

RESULTS AND DISCUSSION

Compatibility study of drug with polymers

Physical mixture of drug and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference of the functional group as the principle peaks of the cefixime trihydrate were found to be unaltered in the drug- polymer physical mixtures, indicating they were compatible chemically. Cefixime trihydrate was determined by FTIR spectra as mentioned in the Figure No 1.

Pre-compression parameters for Cefixime trihydrate tablets

Bulk density was found in the range of 0.476-0.588 g/cm^3 and the tapped density between 0.555 - 0.714 g/cm^3. Using the above two density data, Carr's compressibility index were calculated. The compressibility index was found between 14.9-21.02% and the compressibility and flowability data indicated good flow properties of all powder blends. The better flow property of all powder blends was also evident from angle of repose. The angle of repose was range of 24.12°-29.56°. Angle of repose below 30º indicates good flow property. In the present study all powder blends showed good flow property. The results are shown in Table No: 2

POST- COMPRESSION EVALUATION PARAMETER

Thickness of tablets

All the Dispersible tablet formulations were evaluated for their thickness using Vernier calipers and the results are shown in Table No 3**.**Also the crown diameter of all the formulation was 8 mm

Hardness

All the formulations have an average hardness in between 2.9 to 3.4 kg/cm^2 which was found to be acceptable; because these formulations have to be disintegrated on the tongue between 25 seconds to 1 minute. So excess of hardness is not favored for these formulations. The hardness for F6 (3.37±0.03 Kg/cm^2) was found to be highest of all formulations and for F2 (2.9±0.09 Kg/cm^2) was found to be least and control formulation F1 which shows (2.72±0.10 Kg/cm^2) values respectively for the above parameters and the results were shown in Table No 3

Friability

The average percentage friability for all the formulations were between 0.18% to 0.90%, which was found to be within the limit (i.e. maximum 1%). So the maximum friability was 0.90% and the minimum friability 0.18% observed for F4 and F9 respectively and control formulation F1 which shows 0.38%values respectively for the above parameters and the results were shown in Table No 3

Wetting Time

The average wetting time for all the formulations was in the range of 28 to 39 seconds. The maximum wetting time of 39 seconds and minimum wetting time of 28 seconds were shown by F3 and F9 respectively and control formulation F1 which shows 55 seconds values respectively for the above parameters and the results were shown in Table No 3

Weight Variation

The maximum weight was 150.92±0.41 for F4 and the minimum observed was 149.83±0.36 for F2. The maximum allowed percentage weight variation for tablets 80-250 mg by I.P is 7.5%, and no formulations

are exceeding this limit. Thus all the formulations were found to be comply with the standards given in IP and the results were shown in Table No 3

Drug Content

The range of uniformity of drug content for all formulations was 95.92%w/w to 98.79%w/w respectively and control formulation F1 which shows 93.51%w/w values respectively for the above parameters. Thus all the formulations were found to be comply with the standards given in IP and the results were shown in Table No 3

***In-vitro* disintegration time**

The average *in-vitro* disintegration time for all the formulations were in the range of was 25 to 53 seconds and control formulation F1 which shows 240 seconds. The *in-vitro* disintegration time for formulation F9 was 25 seconds and highest disintegration time was found to be formulation F4 was 53 seconds. So the amount of water uptake and swelling will be more for this formulation F9 and this increased disintegration and the results were shown in Table No 3

Water absorption ratio

The average water absorption ratio for all the formulations were in the range of 50.75% to 64.58% and control formulation F1 shows 39.51% for the above parameters. The water absorption ratio was found to be less in formulationF10 (50.75%) and more water absorption ratio was found to be formulation F9 (64.78%). The results were shown in Table No 4

***In-vitro* drug release studies**

As there is no specific dissolution test available for dispersible tablet of dissolution rate is studied as per USP specifications for conventional tablets with little modification. All the dispersible tablet formulations were evaluated for their *in-vitro* drug and the results are shown in Table 5. The maximum drug release of 91.03% was obtained from formulation F9, and minimum drug release of 74.80% shown by F2. The average drug release immediately after dispersion for all the formulations was in the range of 74.80% to 91.03%. The control formulation F1 drug release was found to be 13.3%. The formulation F9 containing co-processed superdisintegrants sodium starch glycolate:crospovidone (1:3) enhanced the dissolutionrate of fast dispersible tablets.

Discussion about kinetic models

Different kinetic equations (Zero order, First order, Higuchi's, Hixson-Crowell and Koresmeyer-Peppas equation) were applied to interpret the release rate.The release obeyed first order kinetics andthe results of this investigation showed high correlation coefficient among the formulation for first order release and the probable release mechanism was initial diffusion and the value of release exponent (n) was found to be a function of the polymer used and the physicochemical properties of the drug molecule itself and the n values was found to be in the range of 0.113 to 0.348 followed with Fickian (case I) release.

Stability Studies Results

Stability study was conducted for two best formulations selected based on *in-vitro* disintegration time and *in-vitro* drug release.. There was no significant reduction in drug release profile of formulation F9 no significant taste, colour and odour changes. The result was shown in Table 06.There was no significant variation in the drug content and *in-vitro* dissolution profiles after two months stability study for best formulations F9 thus specialized pickings and storage conditions are necessary for the prepared fast dissolving tablets of cefixime trihydrate. The results of the stability are given in the following **Table 06**. There was no significant change in taste, colour and odour. The results found to be satisfactory.

CONCLUSION

Dispersible tablets of Cefixime trihydrate of 150 mg were prepared using co-processed super disintegrants like crospovidone and sodium starch glycolate with different ratio's (1:1, 1:2 and 1:3) vice versa by direct compression method. A total of Eleven formulations were prepared along with control formulation. The following conclusions can be drawn from the results obtained. FTIR studies revealed no chemical interaction of drug with excipients. The tabletting properties like Angle of repose, Bulk density, tapped density; Hausner's ratio and Carr's index of all the formulations were found to be within the standard limits. All the physical characteristics of the formulations like thickness, hardness, friability, wetting time, drug content, water absorption ratio, *in-vitro* disintegration time and *in-vitro* dissolution studies were found to be well within the limits of official standards. All the formulations get disintegrated within a time period of 65 seconds when tested for *in-vitro* disintegration time. The F9 formulation containing sodium starch glycolate and crospovidone in 1:3 ratio was found to have the higher percentage of drug release compared with other formulations. The F2 formulation containing crospovidone and sodium starch glycolate in 1:1 ratio was found to have the lesser percentage of drug release compared with other formulations. All the formulations are found to follow First order drug release and 'n' value indicates that release mechanism follows Fickian release. Stability studies of the tablets in normal humidity conditions were checked and observed that dispersible tablet preparations require specialized packing and storage conditions. It can be concluded from the present work that co-processed super disintegrants of crospovidone and sodium starch glycolate are superior to

Formulation Code	**F1 (CPO)**	**F2 (1:1)**	**F3 (1:2)**	**F4 (1:3)**	**F5 (1:1)**	**F6 (1:2)**	**F7 (1:3)**	**F8 (1:2)**	**F9 (1:3)**	**F10 (1:2)**	**F11 (1:3)**
CefiximeTrihydrate	10	10	10	10	10	10	10	10	10	10	10
Co-Processed Superdisintegrants	-	6	6	6	6	6	6	6	6	6	6
Microcrystallaine cellulose	30	30	30	30	30	30	30	30	30	30	30
Mannitol	101	95	95	95	95	95	95	95	95	95	95
Sodium Saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	3	3	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3	3	3
Total Weight	150	150	150	150	150	150	150	150	150	150	150

Table 1: Formulation development of dispersible tablets of cefiximetrihydrate
***All quantities are in milligrams (mg) only**

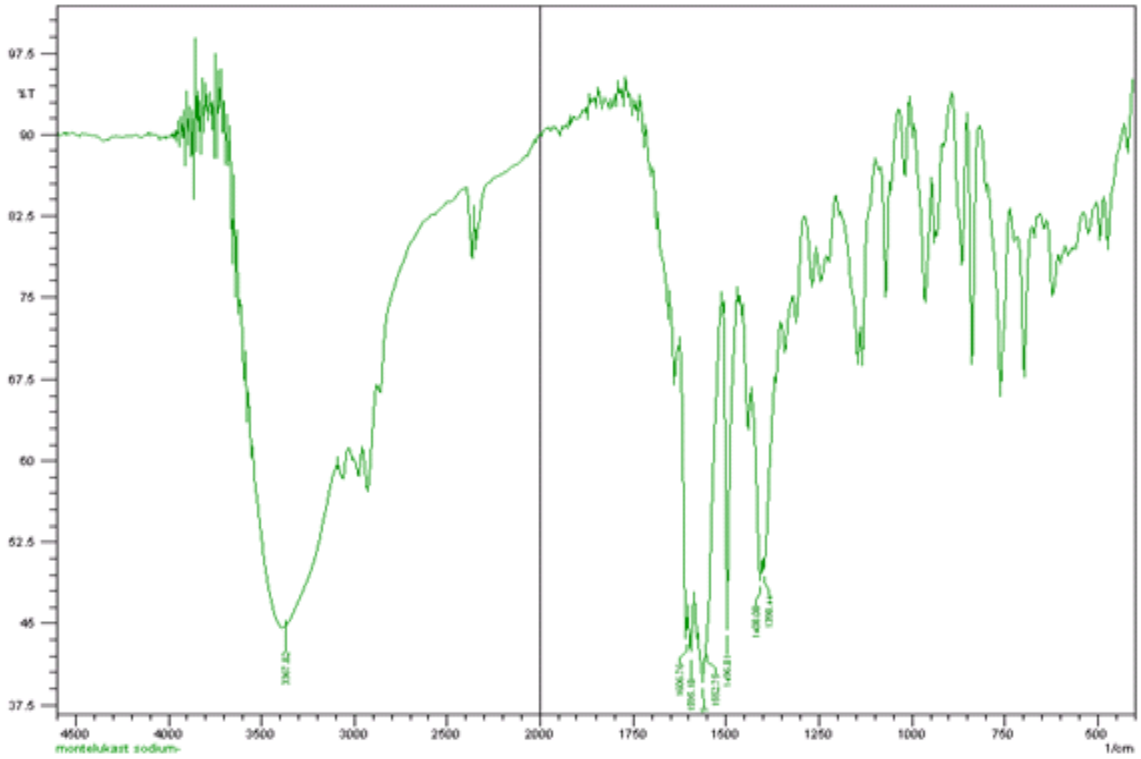
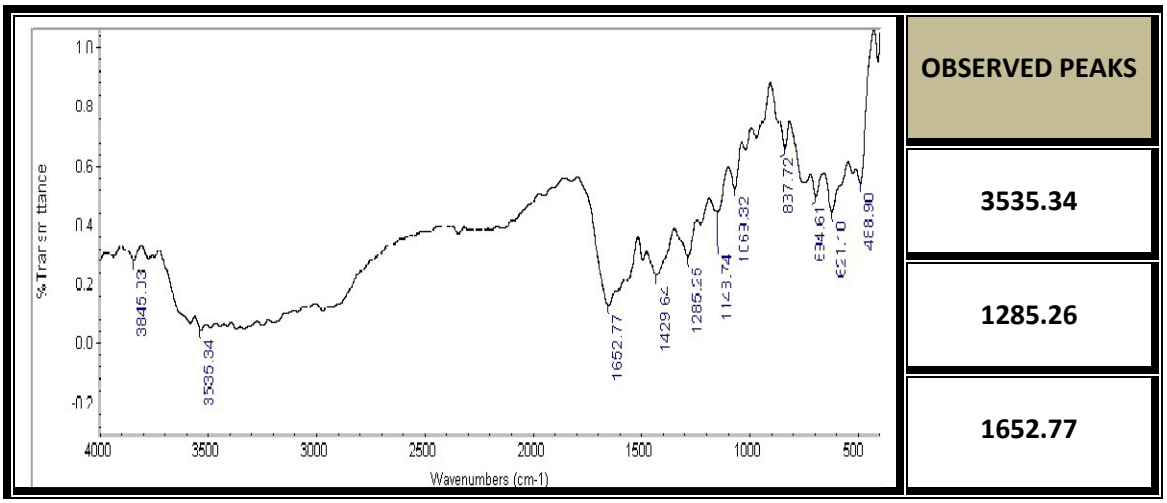
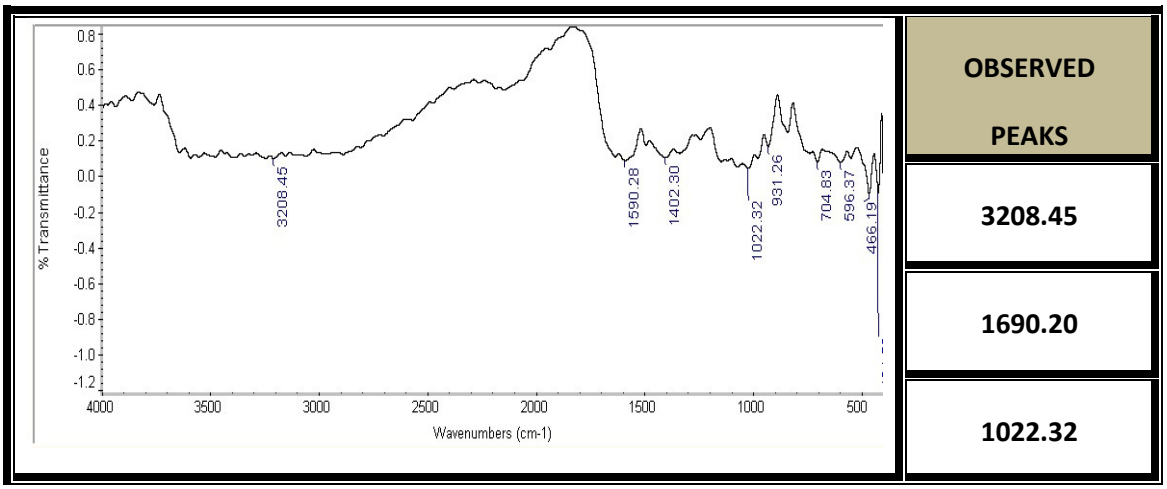


Figure 1: IR spectrum of Cefiximetrihydrate



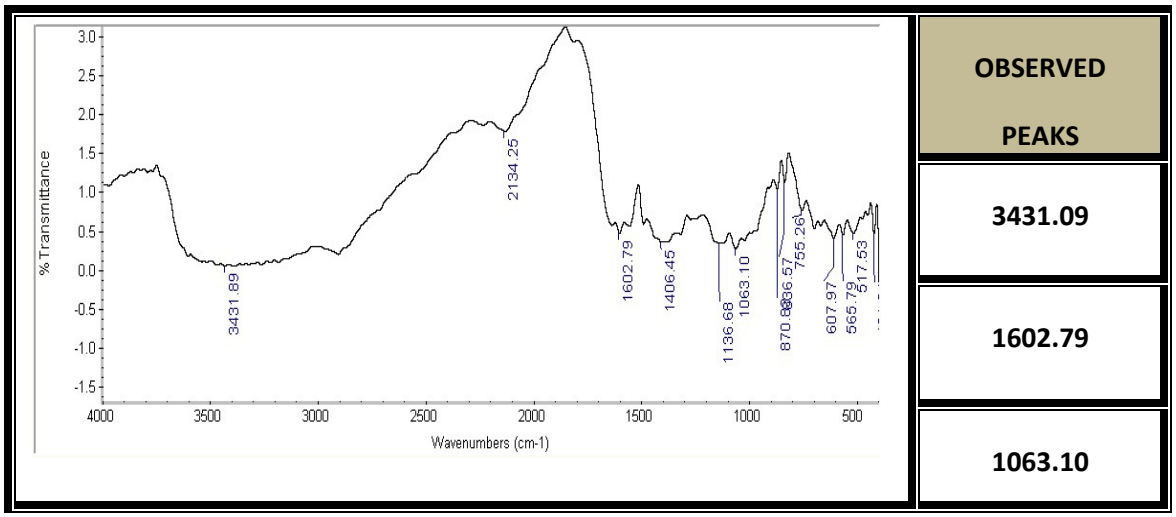
OBSERVED PEAKS
3535.34
1285.26
1652.77

Figure 2: IR spectrum of drug with crospovidone



OBSERVED PEAKS
3208.45
1690.20
1022.32

Figure 3: IR spectrum of drug with sodium starch glycolate



OBSERVED PEAKS
3431.09
1602.79
1063.10

Figure 4: IR spectrum of drug with micro crystalline cellulose

Table- 2: Pre compression parameters of Cefixime trihydrate Granules

Formulation code	Bulk density (g/ml)	Tapped density(g/ml)	Hausner's ratio	Carr'sIndex (%)	Angle of repose(θ)
F1	0.526±0.094	0.666±0.120	1.26	21.02±0.03	29.56±0.04
F2	0.526±0.101	0.666±0.034	1.26	21.02±0.094	29.19±0.067
F3	0.588±0.074	0.714±0.069	1.21	17.64±0.065	27.89±0.051
F4	0.555±0.089	0.666±0.091	1.2	16.6±0.074	26.21±0.079
F5	0.476±0.093	0.588±0.113	1.23	19.04±0.093	27.97±0.084
F6	0.476±0.112	0.555±0.108	1.16	14.23±0.034	27.61±0.099
F7	0.5±0.107	0.588±0.07	1.17	14.9±0.107	25.52±0.021
F8	0.526±0.099	0.666±0.074	1.26	21.02±0.099	25.86±0.044
F9	0.5±0.094	0.625±0.043	1.25	20.0±0.102	24.12±0.042
F10	0.5260.067	0.666±0.021	1.26	20.02±0.074	27.61±0.042
F11	0.5±0.086	0.625±0.09	1.25	20±0.065	25.86±0.042

Table - 03: Post compression parameters for Cefixime trihydrate Tablets

Formulation code	Thickness	Hardness(kg/cm^2)	Friability (%)	Weight variation (mg)	Percentage drug content
F1	3.12±0.01	2.72±0.10	0.38±0.15	149.91±0.22	13.33
F2	3.15±0.03	2.9±0.09	0.76±0.11	149.83±0.36	74.80
F3	3.15±0.03	3.16±0.04	0.77±0.09	150.21±0.49	80.23
F4	3.14±0.02	3.32±0.007	0.90±0.62	150.92±0.41	78.73
F5	3.14±0.01	3.15±0.05	0.41±0.44	150.16±0.32	81.90
F6	3.15±0.04	3.37±0.03	0.92±0.53	149.95±0.91	79.59
F7	3.12±0.01	3.06±0.10	0.37±0.20	150.51±0.99	77.77
F8	3.14±0.02	3.14±0.14	0.40±0.32	150.60±0.60	88.16
F9	3.14±0.01	3.05±0.05	0.18±0.06	150.01±0.59	91.03
F10	3.15±0.01	3.27±0.06	0.33±0.09	150.51±1.02	84.01
F11	3.14±0.01	3.16±0.04	0.66±0.09	150.03±0.59	85.60

Table -4: Evaluation Parameters of Cefixime trihydrate Tablets

Formulation code	Wetting time(sec)	Disintegration time(sec)	Water absorption ratio
F1	55	240	39.95
F2	36	40	50.8
F3	39	49	57.8
F4	36	53	55.84
F5	32	30	59.42
F6	34	33	55.18
F7	33	39	59.65
F8	28	28	62.08
F9	20	24	64.58
F10	31	29	50.75
F11	30	31	54.45

Table 5: *In-vitro* drug release studies of dispersible tablet of Cefixime trihydrate

Time (min)	Percentage drug release (%)											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	MF
0.5	0.5	5.4	31.5	36.5	39.5	39	39.75	37.75	45.25	46.25	40.25	44.75
1	1	6.0	59.42	59.45	56.96	51.96	49.47	51.95	54.50	56.50	53.47	52.74
1.5	1.5	6.57	65.0	68.28	68.28	63.25	60.74	57.99	70.80	73.31	67.76	69.79
2	2	7.07	68.11	73.15	71.91	70.6	68.07	65.56	75.94	80.72	73.64	72.92
3	3	7.53	70.23	75.3	76.05	73.24	72.70	70.92	79.60	83.66	75.54	78.32
4	4	9.67	72.36	76.97	77.47	75.39	75.35	72.31	82.54	85.12	78.45	81.25
6	6	10.9	73.26	78.13	78.39	78.05	77.00	74.95	84.74	87.08	80.38	83.69
8	8	12.0	73.90	79.06	78.56	79.97	78.42	76.61	86.95	89.05	82.32	84.89
10	10	13.3	74.80	80.23	78.73	81.90	79.59	77.77	88.16	91.03	84.01	85.60

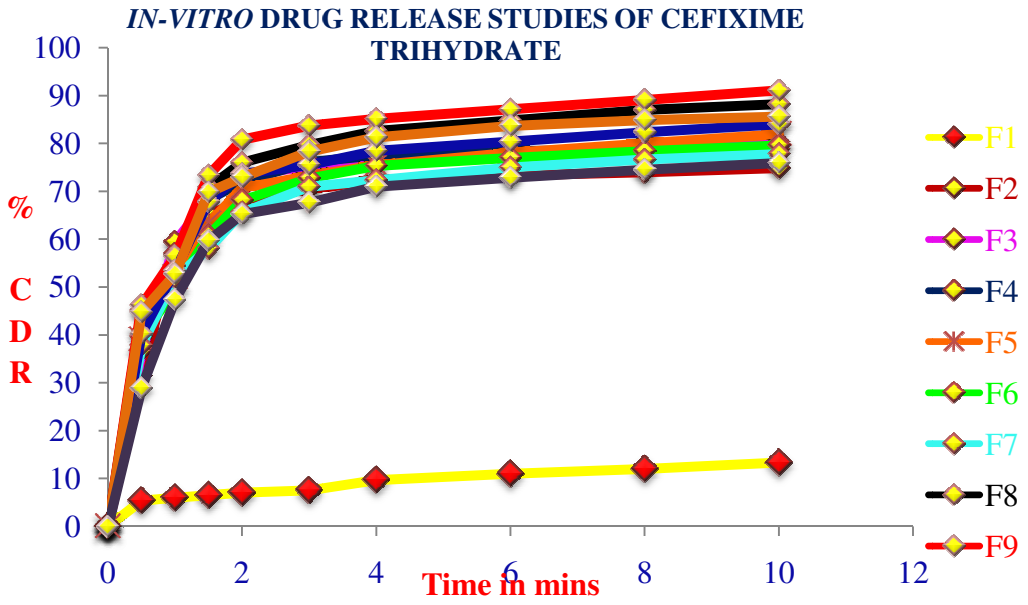


Figure 5: *In-vitro* drug release studies of Cefiximetrihydrate

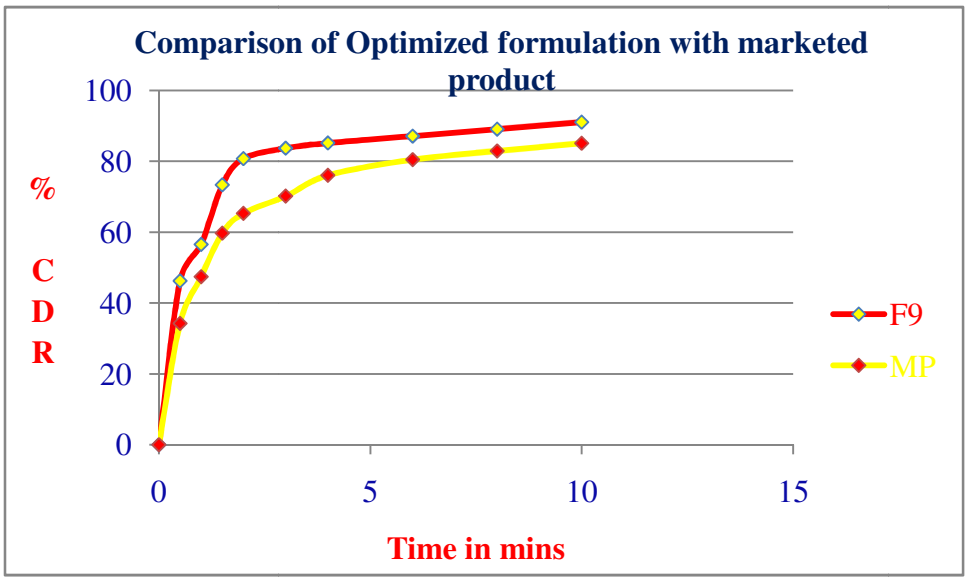


Figure 6:Comparison of Optimized formulation F9 with marketed product

Table 5: Release exponent values and release rate constant values for different formulation

FORMULATION CODE	KORESMEYAR AND PEPPAS		HIGUCHI	HIXON CROWEL	FIRST ORDER	ZERO ORDER
	R^2	n	R^2	R^2	R^2	R^2
F1	0.967	0.348	0.981	0.975	0.975	0.973
F2	0.635	0.130	0.559	0.492	0.534	0.414
F3	0.706	0.122	0.62	0.557	0.604	0.468
F4	0.746	0.113	0.632	0.539	0.572	0.473
F5	0.849	0.129	0.773	0.722	0.769	0.627
F6	0.869	0.128	0.780	0.704	0.740	0.630
F7	0.868	0.127	0.794	0.723	0.760	0.647
F8	0.855	0.119	0.769	0.739	0.797	0.623
F9	0.828	0.117	0.730	0.711	0.779	0.582
F10	0.823	0.126	0.738	0.692	0.744	0.589
F11	0.855	0.119	0.765	0.713	0.760	0.616

R^2=Regression coefficient, **n=** Exponential value

Table 6: Stability studies for best formulations stored at 40ºC/75% RH

TIME	Hardness kg/cm^2		Drug content		*In-vitro* drug release (%CDR)	
	F8	F9	F8	F9	F8	F9
15 days	3.14	3.05	97.87	98.79	88.16	91.03
30 days	3.12	3.05	97.57	98.33	87.91	90.82
45 days	3.13	3.01	97.22	98.05	87.07	90.55
60 days	3.1	3.0	96.9	97.77	86.84	90.00

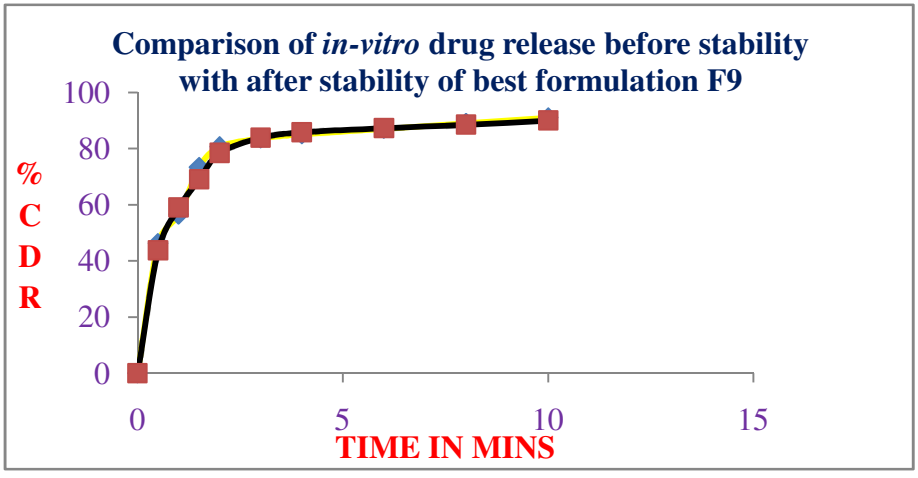


Figure 7:Comparison of *in-vitro* drug release before stability with after stability of best formulation F9

physical mixture of crospovidone and sodium starch glycolate used in Cefixime trihydrae dispersible tablets by direct compression method. The Cefixime trihydrate dispersible tablets were found to have enhanced dissolution rate.

REFERENCES

1. Patel Nibha K, Pancholi SS. An Overview on: Sublingual Route for Systemic Drug Delivery. *Int J Res Pharma Bio Sci.* 2012; 3(2): 913-923.
2. Amir H Shojaei, Sen-lin Zhou, Xiaoling Li. Transbuccal Delivery of Acyclovir (II): Feasibility, System Design and *In-vitro* Permeation Studies. *Int J Pharm Pharma Sci.* 1998; 1(2): 66-73.
3. Khairnar GA, Sayyad FJ. Development of Buccal Drug Delivery System Based on Mucoadhesive Polymers. *Int J Pharm Tech Res.* 2010; 2(1): 719-735.
4. http:// www.unicef.org/ supply/ files/ Dispersible_Tablets.pdf.
5. Setia A, Goyal N, Kansal S. Formulation and evaluation of Ciprofloxacin hydrochloride dispersible tablets using natural substances as disintegrates Der Pharmacia Sinica 2011;2(1):36-39.
6. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of pharmaceutical excipients. 6th ed. Washington. A Joint Publication of American Pharmaceutical Association and The Pharmaceutical Press; 2009: p. 129-33, 208-10, 404-7, 424-8, 608-610, 663-6.
7. Bhanja SB, Ellaiah P, Roy HK, Samal BK, Tiwari S, Murthy KVR. Formulation and Evaluation of Prindopril Sublingual Talets. *Int J Res Pharm Bio Sci.* 2011; 2(3):1193- 98.
8. Sindu Abraham, Basavaraj B V, Bharath S, Deveswaran R, Sharon Furtado, Madhavan V. Formulation and Optimization of Sublingual Tablets of Rabeprazole Sodium. *Int J Pharm Sci Res.* 2010; 5(2):50-54.
9. Bhanja Satyabrata, Hardel Danendra K, Sudhakar Muvala. Formulation and Evaluation of Fast Disintegrating Rosiglitazone Sublingual Tablets. *Int J Pharm Chem Sci.* 2012;1(2): 587-593.
10. Korsemeyer RW, Peppas NA. Macromolecular and modeling aspects of swelling–controlled systems. In: Mansdrofsz, rosemann TJ, ad, Controlled Release Delivery systems. New York. Marcel Dekker; 1983: 77.
11. Shyamala Bhaskaran. Industrial pharmacy. 1st ed. New Delhi. Birla Publications; 2010. pg. 46-69.
12. ICH Q1A (R2) Stability testing guidelines: Stability Testing of new drug substances and products.[online]. [Cited 2008 Nov 10]; Available from: URL:http:/ / www.tga.health.gov.au/ docs/ pdf/ euguide/inch/ 273699r2en.pdf