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DEVELOPMENT AND CHARACTERIZATION OF FAST DISSOLVING TABLETS OF CEPHALEXIN

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ABSTRACT

Background: Cephalexin is a semi synthetic first generation cephalosporin having activity against gram positive and gram negative bacteria. It is primarily used in paediatrics for the treatment of infections of the respiratory tract (e.g. pharyngitis, tonsillitis), skin infections, bone and joint infections, and urinary tract infections. As it is a bitter drug, many works areundertaken to prepare taste-masked fast dissolving tablets of cephalexin by incorporation of artificial sweetener sucralose and pineapple flavor for use in paediatrics. **Objective:** To formulate fast dissolving tablets (FDTs) of cephalexin by wet granulation method. **Materials and Methods:** In this study FDTs were formulated by using superdisintegrant like crospovidone, croscarmellose in different concentrations i.e. 1%, 2.5% and 5%. The formulations were evaluated for weight variation, hardness, friability, wetting time and drug content uniformity. All the formulations showed satisfactory mechanical strength with disintegration time less than 30 seconds. **Results:** The invitro percentage drug release from the formulation F6 containing crospovidone at concentration of 5% was found to be 96% in 10 minutes. The in vitro release data were fitted to different equations and kinetic models to explain release profiles. The correlation coefficient value (r) indicates the kinetic of drug release was first order and the mechanism of drug release was found to follow Fickian transport. **Conclusion:** The results revealed that tablet containing 5% crospovidone (F6) as superdisintegrant had good dissolution profile with shorter disintegration time.

KEYWORDS: Cephalexin, taste-masking, fast dissolving tablets, superdisintegrants.

INTRODUCTION

Fast Dissolving Tablets

Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, orodispersible tablets, rapidmelts, porous tablets, quick dissolving etc. Fast dissolving tablets are novel types of tablets that dissolve/disperse /disintegrate in saliva without water. When put on tongue, disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. The faster the drug into solution, quicker the absorption and onset of clinical effect. The benefits of FDTs are to improve patient compliance, rapid onset of action, increased bioavailability and good stability which make the tabletpopular as dosage form of choice in current market.

The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrollidone (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue their by release the drug in saliva. The technologies used for manufacturing fast-dissolving tablets are freeze-drying, spray-drying, tablet molding, sublimation, sugar-based excipients, tablet compression, and disintegration addition.[1]

Criteria for Fast dissolving Drug Delivery System[2]

- The tablets should not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

Advantages of Fast Dissolving Tablets

Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure and patients who refuse to swallow such as paediatric, geriatric and psychiatric patients.

- Rapid drug therapy intervention.

- Achieve increased bioavailability/rapid absorption through pre-gastric absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travellers and busy people, who do not always have access to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in paediatric patients.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

Methods of Taste Masking[3]

Various methods are available to mask undesirable taste of the drugs.

- Coating of drug particles with inert agents.
- Taste masking by formation of inclusion complexes.
- Molecular complexes of drug with other chemicals.
- Solid dispersion system.
- Microencapsulation.
- Prodrug approach.
- Ion Exchange Resin.

Methods of Preparing Fast Dissolving Tablets[4]

Many techniques have been reported for the formulation of fast dissolving tablets or orodispersible tablets.

- Freeze drying / lyophilisation.
- Tablet Moulding.
- Spray drying.
- Sublimation.
- Direct compression.
- Mass extrusion.

MATERIALS AND METHODS

Materials

Cephalexin was obtained as a gift sample from Sance Laboratories Pvt. Ltd. Kottayam. Microcrystalline cellulose plain, PVP K 30, Crosspovidone, and Croscarmellose sodium were from Yarrow Chem Products, Mumbai. Mannitol, Sucralose and Pineapple flavour from Reltson Healthcare, Pondicherry. Iso Propyl Alcohol, Magnesium Stearate and talc from Nice Chemicals, Ernakulam.

Methods

Preformulation studies

Drug-Excipients Compatibility Studies

FTIR Spectroscopy: Integrity of the drug in the formulation was checked by taking an IR spectrum of the selected formulation along with the drug and other excipients. The pellet of potassium bromide was completely dried at 100°C for one hour and after drying it was thoroughly mixed with the sample in the ratio of 1 part of sample and 100 parts of KBr. The spectra were recorded by using Shimadzu FTIR 8400 spectrophotometer and were compared with standard spectra.[5]

Determination of Solubility

Solubility of cephalexin was determined in various solvents like water, alcohol chloroform and ether. Saturated solution of cephalexin in a various solvent was prepared. 1ml of this solution was subjected to vaporization in an oven until the liquid gets completely evaporated. Remaining weighed for calculating the solubility.[6]

Determination of Melting Point

Determination of melting point was done by capillary method. The finely ground powder was filled into a capillary which has one end closed. Filled capillary tube was inserted into the melting point apparatus and the temperature at which the sample gets melted was noted.

λ_{max} for Pure Cephalexin in Distilled Water

An absorption maximum of cephalexin was determined using distilled water. Solutions ranging from 4-40 μg/ml were scanned from 200-400 nm using UV spectrophotometer.

Calibration Curve for Pure Cephalexin in Distilled Water

Preparation of Standard Stock Solution:- 100 mg of cephalexin was accurately weighed and taken in a 100 ml volumetric flask. The drug was dissolved and diluted to volume with distilled water to get concentration of 1000µg/ml.

Preparation of Working Standard Solution:- 1 ml of the stock solution was withdrawn into a 25 ml volumetric flask and diluted to volume with distilled water to get a concentration of 40µg/ml.

Standard Graph:- From the working standard solution, aliquots of 1, 2, 3, 4, 5, 6. 7, 8, 9, 10 µg/ml were withdrawn into 10ml volumetric flasks and diluted to volume with distilled water to get concentration of 4-40µg/ml. The absorbance of these solutions was measured at 262 nm by UV spectrophotometer, using distilled water as blank. The absorbance values were plotted against concentration to obtain the standard graph.[7]

Preparation of Mouth Dissolving Tablets of Cephalexin

Wet Granulation

Different mouth dissolving tablet formulations were prepared by wet granulation technique. Cephalexin and all other ingredients were passed through sieve no. 20. The required quantities of cephalexin, microcrystalline cellulose, mannitol and starch were weighed and blended in ascending order to get a uniform mixture. The granulating fluid was prepared by dissolving PVP K30 in isopropyl alcohol (5%w/v). Then the granulating fluid was added drop by drop to the blended mixture to get a damp mass which was passed through sieve no.20. The granules were dried at 50-60^{o}C for 15-30 min. Finally the dried granules were again passed through sieve no.20. The granules retained on the sieve were collected and 10% fines were added.

Lubrication

Varying concentrations of superdisintegrants like Crospovidone and Croscarmellose sodium and remaining quantities of mannitol were added to the prepared granules. Talc and magnesium stearate was added in required quantities as glidant and lubricant. Sucralose and pineapple flavour were added as sweeteners and flavouring agent. The mixture was blended thoroughly and the tablets were compressed in 13 mm punch in an eight station rotary punch tablet compression machine. (Table 1)

Table 1: Formulation design of fast dissolving tablets of cephalexin.

Sl. No.	Optimization stage						
	Ingredients (mg)	Formulation code					
		F1	F2	F3	F4	F5	F6
1	Cephalexin Monohydrate (equivalent to 125 mg of the Drug)	130	130	130	130	130	130
2	Croscarmellose	1 %	2.5%	5%	-	-	-
	Crosspovidone	-	-	-	1%	2.5%	5%
3	Micro Crystalline Cellulose Plain	52.8	48	40	52.8	48	40
4	Mannitol	90	90	90	90	90	90
5	Starch	16	16	16	16	16	16
6	P V P K 30	6	6	6	6	6	6
7	Sucralose	2	2	2	2	2	2
8	Talc	8	8	8	8	8	8
9	Magnesium Stearate	12	12	12	12	12	12
10	Pineapple Flavour	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation of Physical Properties of Tablet Blend[8]

Bulk density (D_b)

It is the ratio of total mass of powder and the bulk volume of powder. It was measured by pouring the weighed powder into a graduated measuring cylinder and the volume was recorded. It is expressed in gm/ml and is given by.

$D_b = M/ V_b$

Where, M is mass of powder, V_b is the Bulk volume of the powder.

Accurately weighed quantities of the blended mixture (10 gm) were carefully poured into the graduated cylinder through a funnel and the bulk volume was recorded with and without tapping. The untapped (D_u) and tapped bulk densities (D_t) were calculated from the following formula, weight of blended mixture / untapped volume and weight / tapped volume, respectively.

Carr's index (I) / Percentage compressibility

An important measure that can be obtained from bulk density is the determination of percent compressibility or Carr's index, which is defined as.

$I = (D_t\text{-}D_u/ D_t) \times 100$

Where, D_t is the tapped bulk density of the powder.

D_u is the untapped bulk density of the powder.

Hausner's Ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular

material. It is calculated by the formula

$H = D_t / D_u$

Where, D_t is the tapped bulk density of the powder.

D_u is the untapped bulk density of the powder.

The Hausner's ratio is used as an indication of the flowability of a powder. A Hausner's ratio greater than 1.25 is considered to be an indication of poor flowability.

Angle of Repose

Angle of repose indicates the frictional forces existing between the particles. It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane**.**

$\tan \theta = h/r$

Where, θ = angle of repose

h = height of the powder heap

r = radius

Evaluation of Fast Dissolving Tablets[9]

Weight Variation

The weight variation test was performed on 20 randomly selected tablets after compression and mean weight was determined. None of the tablets deviated from the average weight by ±7.5%.

Hardness test

The Monsanto hardness tester was used to determine the hardness of the tablets. 10 tablets were randomly selected from each formulation and average hardness was determined.

Friability

Tablets were tested for friability using Electrolab (EF2) friabilator. 20 tablets were weighed initially and transferred to the friabilator. The instrument was set to 25 rpm for 100 rotations. The resulting tablets were reweighed and percentage loss was calculated using the formula.

$$\text{Friability} = \frac{(\text{Initial weight} - \text{Final Weight})}{\text{Initial Weight}} \times 100$$

Wetting time

This is carried out to measure the time, which is required for the complete wetting of tablet

formulations. Wetting time of tablet was determined using a simple procedure. A piece of double folded tissue paper was placed in a Petri plate containing 6 ml of simulated salivary pH 6.8 and a drop of amaranth solution was added to it . The tablet was placed on the paper and the time for complete wetting of upper surface of the tablet was measured in seconds.

Drug content

Three tablets of each formulation were weighed and powdered. 240mg of powder equivalent to 100mg of cephalexin was taken. The amount of drug present in a 100mg equivalent amount of powder was determined by dissolving the powder mixture in methanol and distilled water (10:90) for cephalexin determination and UV absorbance was carried out at 262 nm for cephalexin. Drug concentration was determined from their standard graphs.

In-vitro Disintegration test

The in vitro disintegration time was determined using Thermonik tablet disintegration test machine. The limit for disintegration should not be more than 60 seconds at 37°C.

Six tablets were placed individually in each tube of disintegration test apparatus and discs were placed on it. Water bath contained distilled water with temperature maintained constant at 37°C ± 1°C.

In-vitro Dissolution studies

In vitro drug dissolution studies were carried out using Electro Lab dissolution tester USP type II (Model TDT 06PS).

Dissolution medium: Simulated salivary pH 6.8 solution Dissolution volume: 900 ml.

RPM: 75 RPM. Temperature: 37°C ± 0.5°C Samples withdrawn: 5 ml. Initially samples were withdrawn at 2 min interval for 10 min. At appropriate time intervals 5 ml of samples were withdrawn and filtered through Whatman filter paper No 1, the initial volume of dissolution medium was maintained by adding 5 ml of fresh dissolution medium. From the 5 ml withdrawn sample, 1 ml was taken and volume was made up to 10 ml with phosphate buffer (pH 6.8) for determination of cephalexin at λ max of 262 nm by UV-Visible spectrophotometer (UV Visible Spectrophotometer U V -1800 Shimadzu)**.**

Release Kinetics of Optimized Formulation of Cephalexin[10]

The best formulation was selected based on the dissolution study. Drug release mechanism was of the optimized formulation was determined by fitting its drug release data to various

kinetic models.

Zero order release kinetics

Zero order release kinetics refers to the process of constant drug release from a drug delivery device such as oral osmotic tablets, transdermal systems, matrix tablets with low-soluble drugs and other delivery systems. In its simplest form, zero order release can be represented as

$Q = Q_0 + K_0 t$

Where, Q is the amount of drug released or dissolved (assuming that release occurs rapidly after the drug dissolves), Q_0 is the initial amount of drug in solution (it is usually zero), and K_0 is the zero order release constant.

First order release kinetics

The rate laws predicted by the different mechanisms of dissolution both alone and in combination, have been discussed by Higuchi.

$\text{Log } C = \text{Log } C_0 - kt / 2.303$

Where, C_0 is the initial concentration of drug and K is first order constant. The equation in resemblance to the other rate law equations, predicts a first order dependence on the concentration gradient (i.e. $C_s - C_t$) between the static liquid layernext to the solid surface and the bulk liquid.

Higuchi Model

Higuchi tried to relate the drug release rate to the physical constants based on simple laws of diffusion. Release rate from both a planar surface and a sphere was considered. Higuchi was the first to derive an equation to describe the release of a drug from an insoluble matrix as the square root of a time-dependent process based on Fickian diffusion.

$Q_t = k_H (t) 0.5$

Where, Q_t is the amount of drug released in time t, and k_H is the release rate constant for the Higuchi model.

Korsemeyer-Peppas Model

The drug release data of optimized formulation was plotted in accordance with Korsemeyer - Peppas model. Korsmeyer et al (1983) derived a simple relationship which described drug release from a polymeric system. To find out the mechanism of drug release, first 60% drug release data was fitted in Korsmeyer–Peppas model.

$M_t/M_\infty = Kt\ n$

Where, M_t/M_∞ is fraction of drug released at time t, k is the rate constant and n is the release exponent. The n value is used to characterize different release mechanisms as given in table for cylindrical shaped matrices.

Hixson- Crowell model

The Hixson-Crowell cube root law describes the release from systems where there is a change in surface area and diameter of particles or tablets. For a drug powder consisting of uniformly sized particles, it is possible to derive an equation that expresses the rate of dissolution based on the cube root of the particles.

$Q_0^{1/3} - Q_t^{1/3} = K_{HC}\ t$

Where, Q_t is the amount of drug released in time t, Q_0 is the initial amount of the drug in tablet and K_{HC} is the rate constant for Hixson-Crowell rate equation.

RESULTS AND DISCUSSION

The results of granules evaluation suggest that the granules exhibits good flow properties as the angle of repose values were less than 30^o. A good packing ability of the granules was indicated by Carr's compressibility index and Hausner's ratio.

FTIR studies conducted on cephalexin and physical mixture of cephalexin and crospovidone and croscarmellose showed that there was no marked interaction between cephalexin and superdisintegrants employed croscarmellose and crospovidone. Solubility of the drug in water, alcohol, chloroform ether, and methanol was examined and found to be in conformity with pharmacopoeial specifications. The melting point of pure cephalexin was found to be 191ºC. The absorbance of standard cephalexin solutions from concentrations 4-40µg/ml were measured at 262nm.

All the formulations prepared had hardness in the range of 3 to 4 kg/cm^2 and friability was in the range of 0.24 to 0.43 % and drug content was in the range of 96.41% to 99.42%. The weight and drug contents of all the tablets were found to be uniform and complied with pharmacopoeial limits. Optimized formulation F6 containing 5% crospovidone as superdisintegrant showed least wetting time of 14 seconds as compared to formulation F3 containing 5% croscarmellose which showed wetting time of 18 seconds.

In vitro drug release study was done in phosphate buffer pH 6.8. Formulation F1 containing

1% croscarmellose showed a drug release of 80% as compared to formulation F2 containing 2.5% croscarmellose which showed 87.2% release after 10 min. Formulation F3 containing 5% croscarmellose showed increase in drug release upto 90.5% in 10 min. Formulation F4 containing 1% crospovidone and F5 containing 2.5% crospovidone showed 76.8% and 88.9% drug release, respectively. FormulationF6 containing crospovidone 5% showed the release of 96.5% in 10 min. Hence formulation F6 showed better result when compared to all other formulations and therefore selected as the optimized formulation.

The drug release kinetics and mechanism of drug release was studied for the optimized formulation by fitting the in-vitro dissolution data into different kinetic models like zero order, first order, Higuchi model and Korsemeyer- Peppas model. From the kinetic study the drug release mechanism was first order and follow Fick's law of diffusion. Optimized formulation F6 showed cephalexin release best fittedinto first order.

Compatibility Analysis (Ftir)

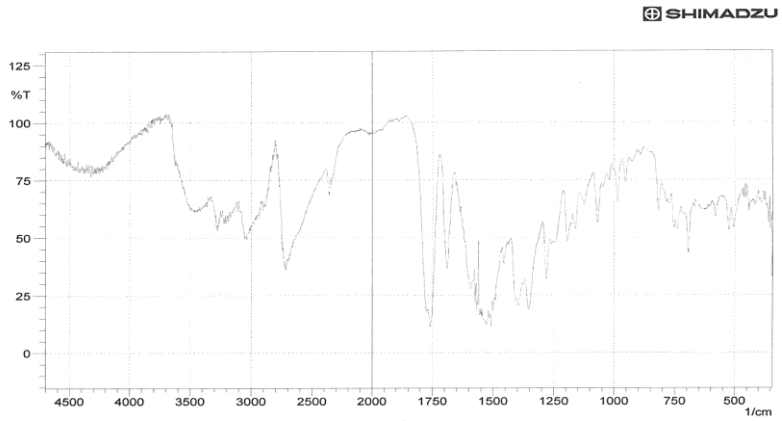

Fig. 1: IR spectra of Cephalexin.

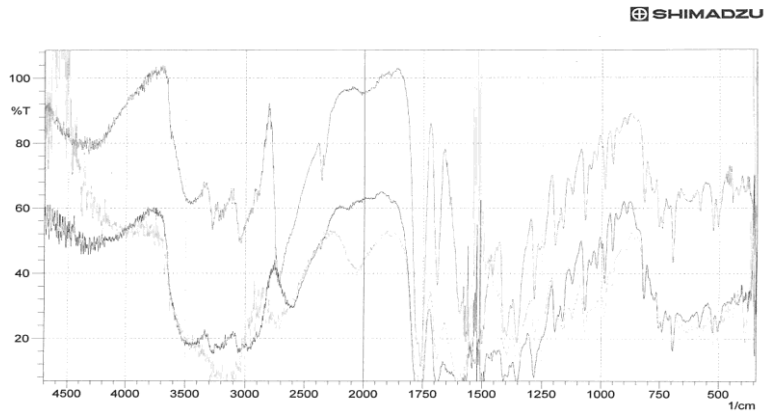

Fig. 2: IR spectra of physical mixture of cephalexin, crospovidone and croscarmellose.

Table 2: Solubility profile of cephalexin.

Solvent	Solubility
Water	Slightly soluble
Alcohol	Insoluble
Chloroform	Insoluble
Ether	Insoluble

Table 3: Standard calibration curve data of cephalexin in distilled water.

SI No	Volume taken in ml	Concentration in mcg/ml	Absorbance
1	1	4	0.130
2	2	8	0.232
3	3	12	0.348
4	4	16	0.462
5	5	20	0.559
6	6	24	0.664
7	7	28	0.765
8	8	32	0.885
9	9	36	1.009
10	10	40	1.12

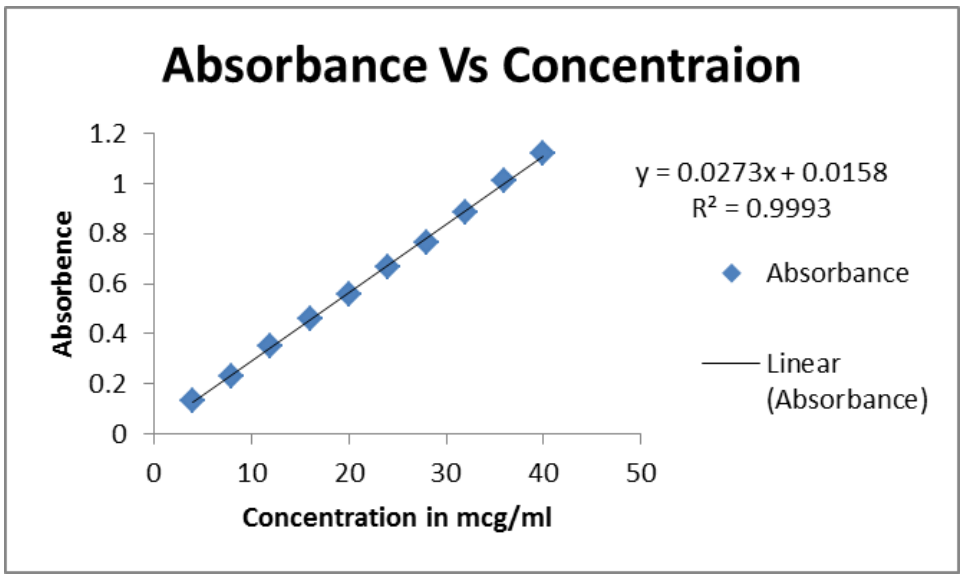

Fig 3: Standard calibration graph of Cephalexin.

Table 4: Preformulation studies of blends.

Parameters	F1	F2	F3	F4	F5	F6
Bulk density (g/ml)	0.5221	0.5426	0.5586	0.5579	0.5432	0.5514
Tapped density (g/ml)	0.6685	0.6742	0.6914	0.6889	0.6875	0.6845
Carr's index(%)	21.8	24.25	23.77	20.94	20.98	19.44
Hausner's ratio	1.28	1.24	1.23	1.23	1.26	1.24
Angle of repose	26.9	27.45	29.32	28.46	28.78	26.72

Table 5: Evaluation of fast dissolving tablets of Cephalexin.

Parameters	F1	F2	F3	F4	F5	F6
% weight variation	1.6	0.98	1.5	1.1	0.89	1.8
Hardness (kp)	3.4	3.7	3.6	4.2	3.6	3.8
Friability (%)	0.38	0.41	0.43	0.24	0.36	0.28
Disintegration time (sec)	25	26	22	24	26	19
Wetting time(sec)	28	24	21	26	21	14

Table 6: Evaluation of drug content of fast dissolving tablets of Cephalexin.

Serial No	Formulations	Drug Content*(%)
1	F1	96.41
2	F2	94.85
3	F3	97.45
4	F4	95.78
5	F5	96.51
6	F6	99.42

Table 7: In-vitro dissolution studies of optimized formulation F6(5% Crospovidone).

Time	Absorbance	Concentration (mcg/ml)	Amountin 5ml(mg)	Amount in 900ml(mg)	Correction factor	Cumulative release	% Release
0	0.030	0.5555	0.0277	5.0000	0	5.0000	4.0000
2	0.145	4.8148	0.2407	43.3333	0.0277	43.3611	34.6888
4	0.282	9.8888	0.4944	89.0000	0.5222	89.5222	71.6177
6	0.345	12.2222	0.6111	110.0000	1.1333	111.1333	88.9066
8	0.357	12.6666	0.6333	114.0000	1.7666	115.7667	92.6133
10	0.369	13.1111	0.6555	118.0000	2.4222	120.4222	96.3377

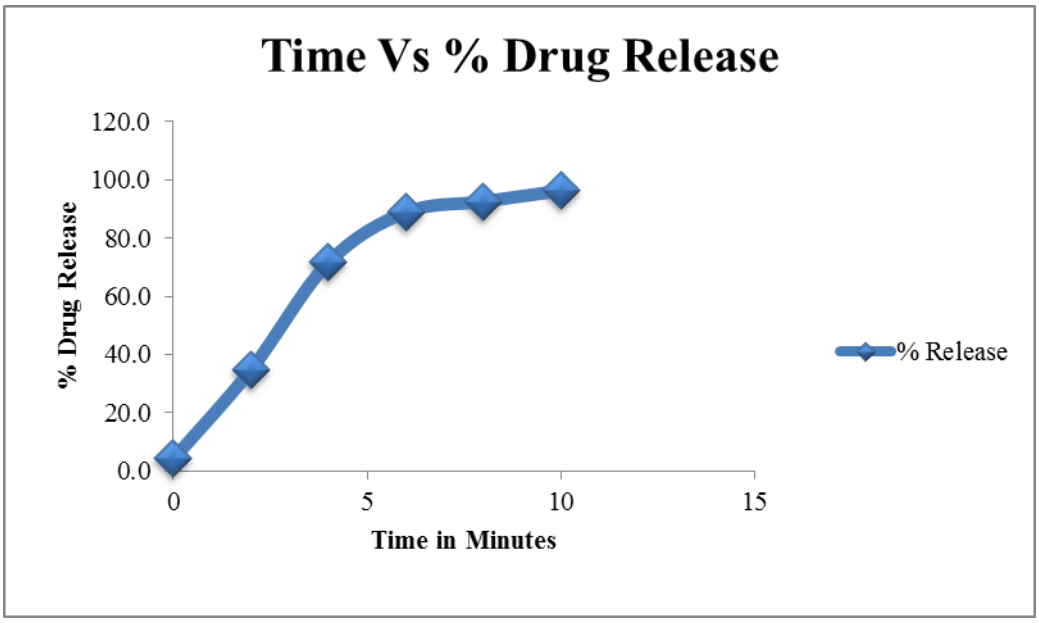

Fig 4: In-vitro dissolution graph of optimized formulation F6.

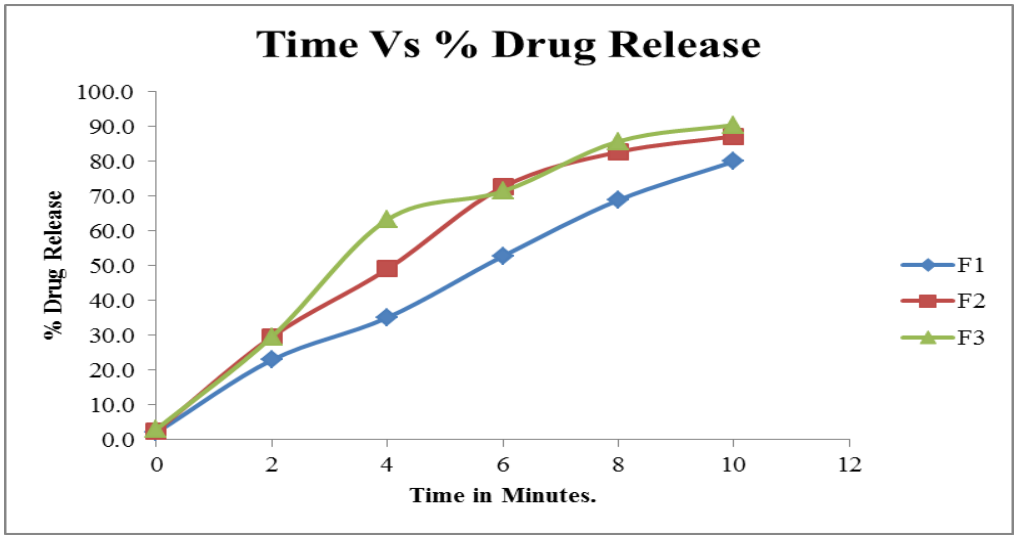

Fig 5: Comparison of In Vitro Drug Release of F1, F2 and F3.

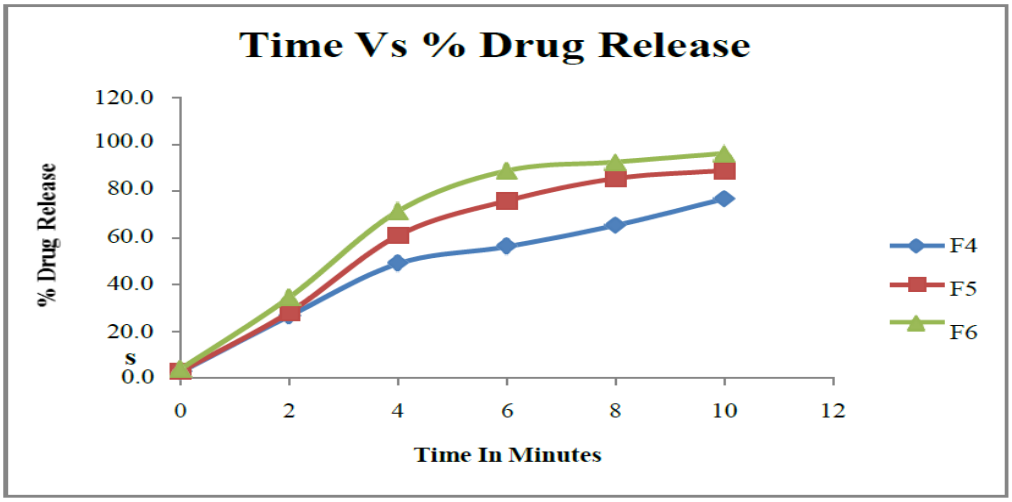

Fig 6: Comparison of In Vitro Drug Release of F4, F5 and F6.

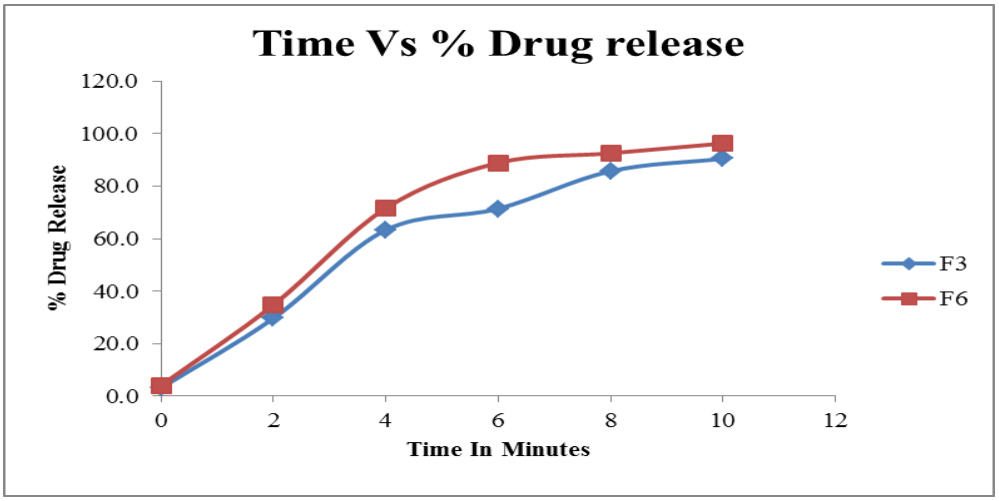

Fig.7: Comparison of In Vitro Drug Release of F3 and F6.

Table 8: First order release kinetic study of optimized formulation F6.

Time in Minutes	Log % Drug Retained
0	2.0
2	1.8
4	1.5
6	1.0
8	0.9
10	0.6

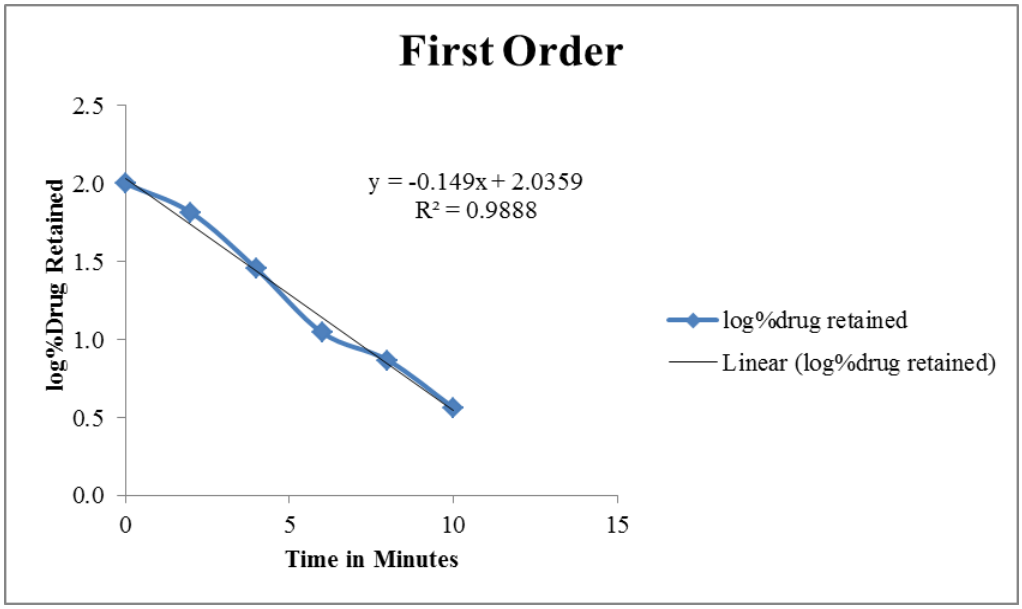

Fig. 9: First order release plot for F6.

CONCLUSION

In the present study, an attempt was made to prepare and evaluate taste masked fast dissolving tablets of Cephalexin. It can be concluded that FDTs prepared by wet granulation method by using 5% crospovidone as superdisintegrants, sucralose and pineapple flavor as taste masking agents showed the maximum drug content, least disintegration time, least wetting time, and maximum drug release.

All the six formulations showed a drug release of more than 75% in 10 minutes. Optimized formulation F6 (5% crospovidone) showed a drug release of 96.3% in 10 minutes. Hence the formulation F6 has the maximum drug content.

After performing the kinetic study, release mechanism was found to be first order and followed by Fick's diffusion. Thus it can be concluded that taste masked fast dissolving tablets (FDTs) containing 5% crospovidone as superdisintegrant exhibited excellent mouth melting as well as release characteristics when prepared by wet granulation method. This

property of mouth dissolving tablets is beneficial for children who are having difficulty in swallowing. Studies have shown promising results, further, there exists a scope for animal studies.

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Conflict of interest

The authors of this study declare that there is no conflict of interest in the present research work.

REFERENCES

1. D Debjit Bhowmik, Chiranjib. B, Krishnakanth, Pankaj, R. Margret Chandira, Fast Dissolving Tablet: An Overview Journal of Chemical and Pharmaceutical Research, 2009; 1(1): 163-177.
2. Jigar V soni, Nirav R. Patel, Dr. Praful D. Bharadia, Vikram M. Pandya, Darshan M. Modi Different Methods and Evaluation Parameters of Fast Disintigrating Tablets IJPI's Journal of Pharmaceutics and Cosmetology, 2011; (1): 4.
3. Ramesh Kannuri, Threveen Challa, Haeesha Chamarthi, Taste Masking and Evaluation Method For Oridispersible Tablets Int. J. Pharma & Ind. Res, 2011; 01(03): 200-210.
4. Jigar V soni, Nirav R. Patel, Dr. Praful D. Bharadia, Vikram M. Pandya, Darshan M. Modi . Different Methods and Evaluation Parameters of Fast Disintigrating Tablets IJPI's Journal of Pharmaceutics and Cosmetology, 2011; (1): 4.
5. www.pmda.go.jp/english//pharmacopoeia/pdf/sixteenth_edition/ JP16%20IR%20A%20to%20C.pdf.
6. https://pubchem.ncbi.nlm.nih.gov/compound/Cephalexin-monohydrate.
7. Priya Sharma, Design and Development of Mouth Dissolving Tablet(MDTs) of Cephalexin, 63.
8. Mark Gibson, Pharmaceutical Preformulation and Formulations, 369.
9. Fiese E F, Hagen T A, Lachman L, Liberman H A, Karnig J.L. Theory and practice of industrial pharmacy, 3rd edition, Varghese publishing house, Mumbai, 1987; 300.

10. Ramteke K.H., Dighe P.A., Kharat A. R1., Patil S.V2 Mathematical Models of Drug Dissolution: A Review Sch. Acad. J. Pharm, 2014; 3(5): 388-396.