Int. J. Sci. R. Tech., 2025 2(1)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Formulation and Optimization of Effervescent Tablets by Design Of Experiments

Sudarshan Mirgal*, Dr. Bharat Tekade, Dr. Mohan Kale
Department of Pharmaceutics, Konkan Gyanpeeth Rahul Dharkar college of pharmacy and Research institute, Karjat, Maharashtra, India

ABSTRACT
Effervescent tablets are a popular dosage form known for their ease of administration, particularly for patients who have difficulty swallowing conventional tablets. The objective of this study was to formulate and evaluate Cefdinir effervescent tablets using the principles of the Design of Experiments (DOE). Cefdinir is a third-generation cephalosporin antibiotic, commonly used to treat bacterial infections, but it faces challenges in oral bioavailability due to poor solubility.The formulated tablets were evaluated for their physical and chemical properties, including hardness, friability, weight variation, and dissolution rate, using standard pharmacopeial methods. In addition, the optimization of formulation parameters was analyzed through statistical analysis to identify the most influential factors and their interactions. The outcome of this study was the identification of an optimal formulation for Cefdinir effervescent tablets, providing enhanced solubility and faster onset of action, which is essential for improving patient compliance and therapeutic efficacyIn conclusion, the application of DOE in the development of Cefdinir effervescent tablets allowed for a systematic approach to optimize the formulation, resulting in a high-quality dosage form with improved drug release and stability profiles. This study highlights the importance of formulation design in the development of novel drug delivery systems and the potential benefits of effervescent tablets in enhancing the therapeutic performance of antibiotics like Cefdinir.
Keywords: Cefdinir, Effervescent Tablets, Optimization, Dissolution Rate, Bioavailability, Excipients.

INTRODUCTION
Oral drug administration has been the predominant route for drug delivery. During the past two decades, numerous oral delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a predetermined and controlled rate. From a pharmacokinetic point of view, the ideal sustained and controlled release dosage form should be comparable with an intravenous infusion, which supplies continuously the amount of drug needed to maintain constant plasma levels once the steady state is reached.Although some important applications, including oral administration of peptide and protein drugs, can be used to prepare colonic drug delivery systems, targeting drugs to the colon by the oral route. More often, drug absorption is unsatisfactory and highly variable among and between individuals, despite excellent in vitro release patterns. The reasons for this are essentially physiological and usually affected by the GI transit of the form, especially its gastric residence time (GRT), which appears to be one of the major causes of the overall transit time variability.Modified release systems, on the other hand, have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients (APIs) and patient compliance, as well as reducing side effects. Oral modified release delivery systems are most commonly used for

- delayed release (e.g., by using an enteric coating);
- extended release (e.g., zero-order, first-order, biphasic release, etc.);
- programmed release (e.g., pulsatile, triggered, etc.) and
- site specific or timed release (e.g., for colonic delivery or gastric retention). Extended, sustained or prolonged release drug delivery systems are terms used synonymously to describe this group of controlled drug delivery devices, with predictability and reproducibility in the drug release kinetics.

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Basic Gastrointestinal Tract Physiology

Anatomically the stomach is divided into 3 regions: fundus, body and antrum(pylorus). The proximal part made of fundus and body ats as a reservoir for undigested material whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. During the fasting state an interdigestive series of electric events takes place, which cycle both through stomach and intestine every 2 to 3 hours. This is called inter digestive mylo-electric cycle or migrating myoelectric cycle (MMC) which is further divided into following 4 phases as described by Wilson and Washington.

Phase I (basal phase) lasts from 40 to 60 min with rare contractions.

Phase II (pre burst phase) lasts for 40 to 60 min with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increase gradually.

Phase III (burst phase) lasts for 4 to 6 mins. It includes intense and regular contractions for short period. It is due this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.

Phase IV lasts for 0 to 5 mins and occurs between phase III and 1 & 2 consecutive cycles. Scintigraphy studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically 2 complications: short gastric residence time and unpredictable gastric emptying rate.

AIM & OBJECTIVE

Aim

Preparation and Evaluation of effervescent tablets by DOE (Gastro Retentive Drug Delivery System) for Selected Drug Effervescent formulations are given in solution form; which are without difficulty consumed that's why they are chosen over conventional oral solid dosage form, which have a problematical for paediatric and geriatric patients (Huang et al. 2547-53; Hassan and Aboloyoun 197-203). The effervescent formulations are in liquid form, there is not get in touch with gastrointestinal tract. Due to that it decreases gastric irritation while passing through stomach and intestine. The second benefit of the effervescent formulation is that, all amount of drug goes in to the stomach (Bodmeier, Swarbrick and Boylan 1454-65; Mohapatra, Parikh and Gohel 177).

Objectives

- To Prepare Cefdinir GRDDS formulation
- To optimize the formulation of effervescent tablets by using response surface method
- To Evaluate Cefdinir GRDDS formulation
- To carryout stability studies
- To carryout in vitro drug release and in vivo studies

MATERIALS & METHODS

List Of Chemicals With Brand And Supplier

Table 1: List Of Chemicals With Brand And Supplier

Sr.no	Drug/excipients	Name of supplier
1	Cefdinir	Hetero labs, Hydrabad
2	HPMC	A.R Chemical.
3	Eudragit	A.R Chemical.
4	Ethyl cellulose	A.R Chemical.
5	Sodium alginate	A.R Chemicals.
6	Gum karaya	A.R Chemicals,
7	Xanthum gum	A.R Chemicals.
8	Na CMC	A.R Chemicals.
9	Citric acid	A.R Chemical.
10	Microcrystalline cellulose	A.R Chemical.
11	Sodium bi carbonate	A.R Chemical.
12	Magnesium stearate	A.R Chemical.
13	Talc	A.R Chemical.

LIST OF EQUIPMENTS

Table 2: List of Equipments

S.no	Instruments	Name of supplier
1	Digital balance (BS223S)	Sartorius, India
2	Hydraulic pellet press (TYPE KP)	Kimaya engineers, Mumbai
3	Sieve (#18)	Hicon standard sieves, Mumbai
4	UV Visible spectrophotometer (UV-1800)	Lab India
5	FTIR(IRAffinity-1)	Bruker, Japan
6	Dissolution tester TDT06L (USP)	Lab India, India
7	Pfizer hardness tester (USP 1217)	Electrolab, India
8	Roche Friabilator (USP)	Electrolab, India
9	Tap density tester (ETD 1020)	Electrolab, India
10	DSC-60(TA-60)	Shimadzu, Japan
11	Mini-Rotary compression machine	Remi, India

Preformulation Studies

Organoleptic Characteristic:

The colour, Odor, and taste of the drug were characterized and recorded using descriptive terminology.

Solubility studies

Solubility study of Model drug in different media:

Solubility studies were performed by taking required quantity of drug in 10 mL of different buffers at various pH conditions (pH 1.2, pH 4.5acetate, pH 6.8phosphate buffer, and water) separately up to its saturation and subjected to mechanical shaking at 100 rpm for 24 hrs. The resultant dispersions were collected and filtered through 0.2 µm filters and the concentration of drug was determined from absorbance at 290 nm.

Determination of absorption maximum (λmax):

Cefdinir was weighed accurately 10 mg and transferred to 100 ml volumetric flask, dissolved in phosphate buffer pH 6.8 and the final volume was made up to 100 ml with phosphate buffer pH 6.8 to get a stock solution (100µg/ml). From the stock solution, 1 ml was pipette out in 10 ml volumetric flask and the final volume was made up to 10 ml with phosphate buffer PH 6.8 to get 10µg/ml. Then this solution was scanned at 200-400nm in UV-Visible double beam spectrophotometer (UV-3200, Labindia, India) to get the absorption maximum (λmax).

Construction of Cefdinir calibration curve with phosphate buffer pH 6.8:

100mg of Cefdinir was dissolved in 100ml of phosphate buffer pH 6.8 to give a concentration of 1mg/ml (1000µgm/ml). From the above standard solution (1000µgm/ml) 10 ml was taken and diluted to 100ml with phosphate buffer pH 6.8 to give a concentration of 100µgm/ml. From this stock solution aliquots of 0.2, 0.4, 0.6, 0.8 and 1ml were pipette out in 10ml volumetric flask and the volume was made up to the mark with phosphate buffer pH 6.8 to produce concentration of 2, 4, 6, 8 and 10 µgm/ml respectively.

Calibration Curve of model drug in 0.1N HCl

10 mg of model drug was dissolved in 100 ml of 0.1N HCl (pH1.2) to obtain the working standard of 100 µg/ml. Aliquots of 0.2ml to 0.7ml from the stock solution representing 2 to7µg/ml of drug were transferred to 10 ml volumetric flask and the volume was adjusted to 10 ml with 0.1N HCl. Absorbance of the above solutions was taken at λmax 290nm against the blank solution prepared in the same manner without adding the drug.

Drug- excipient compatibility studies by FT-IR:

Compatibility of the drug and formulation is an important pre-requisite for formulation. Therefore, DSC and FTIR spectral analysis of pure drug levosalbutamol and physical mixture of levosalbutamol and super disintegrant were carried out. FTIR spectra of physical mixtures (1:1) of levosalbutamol and various excipients, as well as the formulation were performed to find out any possible drug excipient interaction by ATR method using FTIR spectrophotometer.

Flow Properties of Effervescent Powder:

Bulk Density:

Bulk density was determined by measuring the volume of a known mass of powder sample that has

been passed through a screen into a graduated cylinder. Approximately 10gm of test sample, M was introduced into 25 mL dry measuring cylinder without compacting. The powder was levelled carefully without compacting and read the unsettled apparent volume V0, to the nearest graduated unit. Bulk density was calculated, in g/mL, by the formula. Bulk density is used to determine the amount of drug that occupies the volume in mg/mL. Weighed quantity of API was transferred into 100 ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was measured by using formula.

$$\text{Bulk density} = \frac{M}{V0}$$

Generally, replicate determinations are desirable for the determination of this property.

Tapped density:

Tapped density was achieved by mechanically tapping a measuring cylinder containing a powder sample. After measuring the initial weight and volume, the cylinder was mechanically tapped, and volume readings were taken until little further volume change is observed. It is the ratio of mass of powder to the tapped volume. Tapped volume is the volume occupied by the same mass of powder after a standard tapping of a measure. Cylinder containing the sample was tapped mechanically by raising the cylinder and allowing it to drop under its own weight using a suitable mechanical tapped density tester that provides a fixed drop of 14 ± 2 mm at a nominal rate of 300 drops per minute. It was repeated in increments of 1250 taps, as needed, until the difference between succeeding measurements is less than 2%. The tapped density was calculated, in g/mL, by the formula:

$$\text{Tapped density} = \frac{M}{Vf}$$

Generally, replicate determinations are desirable for the determination of this property.

Carr's Index (Compressibility):

The Compressibility Index and Hausner Ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. It is indicated as Carr's compressibility index and is calculated as follows.

Carr's index = [Tapped density - Bulk density/Tapped density] X 100

Hausner's ratio:

It is measurement of frictional resistance of the drug. It is the determined by the ratio of tapped density and bulk density. Hausner's ratio is defined as a ratio of a tapped density to bulk density. It is a measure of relative importance of interparticulate interactions. A Hausner's ratio greater than 1.25 is considered to be an indication of poor flowability. Method Tapped density and bulk density were measured and the Hausner's ratio was calculated using the formula,

Hausner's ratio = Tapped density / Bulk density

Angle of Repose:

The angle of repose has been used to characterize the flow properties of solids. Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles. Angle of repose was formed on a fixed base with a retaining lip to retain a layer of powder on the base. The base should be free of vibration. The height of the funnel was varied to carefully build up a symmetrical cone of powder. Care should be taken to prevent vibration as the funnel is moved. The funnel height should be maintained approximately 2–4 cm from the top of the powder pile as it is being formed in order to minimize the impact of falling powder on the tip of the cone. Angle of repose was determined by measuring the height of the cone of powder and calculating the angle of repose.Angle of repose was then calculated with the use of the following formula:

$$\tan \theta = h / r$$

where, θ= angle of repose; h= height of the pile; r = average radius of the powder cone

Preparation of tablets

Direct compression technique

Different matrix embedded formulations of Cefdinir were prepared by direct compression method using varying proportion of polymers either alone or in combination. The composition of various formulations of the tablets with their codes is listed in Table. The ingredients were passed through a 60#. Developed tablets were evaluated for different evaluation parameters as per IP (Indian Pharmacopoeia 43). Magnesium stearate was added as lubricant; the appropriate amount of the mixture was weighed and then compressed using a Ten station

rotary press at a constant compression force equipped with a 10-mm flat-faced punches at a compression force required to produce tablets. All the tablets were stored in airtight containers for further study.

Experimental Design

To study the effect of factors, identified during preliminary trials, on the various properties of effervescent tablets, experiments were planned as per box Behnken design. Design Expert® software (trial version 7.1.2, Stat-Ease, Inc., Minneapolis, MN) was used to graphically express the influence of each factor on the response by generating the response surface plots [11]. The amount of sodium bicarbonate (X1), amount of tartaric acid (X2) and amount of fumaric acid (X3) were selected as independent variables. The dependent response variables measured were disintegration time, amount of carbon dioxide and % drug release after 5 min. The levels of independent variables in coded as well as in actual form are shown in table and composition of design batches are shown in table. The polynomial equation created by design is as follows:

$$Yi=b0+b1X1+ b2X2+ b3X3+ b12X1X2+ b23X2X3+ b13X1X3 +b11X1\ 2 + b22X2\ 2 + b33X3\ 2 \quad (1)$$

where Yi is the dependent variable; b0 is the intercept; b1, b2, b3, b12, b23, b13, b11, b22 and b33are the regression coefficients; and X1, X2 and X3 are the independent variables. All the batches were prepared and evaluated in triplicate (n=3). Selection of optimized formulation was done after considering the results of dependent variables of the experimental design batches. The batch with lower disintegration time and higher carbon dioxide and drug release in 5 minutes will be considered as optimized batch. The selected dependent variables are correlated with each other because higher amount of released carbon dioxide results in faster bursting of tablets and hence lower disintegration time and faster drug release property.

Table 3: Experimental design of Cefdinir formulations

Independent variables	Levels		
	Low	Medium	High
Sodium bicarbonate (X1)	50	75	100
Tartaric acid (X2)	20	30	40
Fumaric acid (X3)	30	40	50
Dependent variables			
Y1= Disintegration time			
Y2= Drug release after 5 min			
Y3= swelling studies			

Post-compression physicochemical evaluation of Cefdinir tablets

Visual inspection

The prepared tablets were inspected visually for general tablet deformities. The tablets were smooth with uniform in size, shape and colour. There was no lamination or chipping was observed in all the tablets which indicated that the tablet instrumentation was compatible with the powder blends and resulting in good tablet characteristics.

Weight variation

Formulated tablets were tested for weight uniformity, 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. The percent weight variation was calculated by using the following formula.

$$\%\ \text{Weight Variation} = \frac{\text{Average Weight - Individual Weight}}{\text{Average Weight}} X100$$

Hardness

The hardness of the tablet was measured by Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. As the spring was compressed a pointer ride along a gauge in the barrel to indicate the force. The hardness was measured in terms of kg/cm2.

Friability

The Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula.

$$\text{Friability} = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} X100$$

Drug content uniformity

Ten tablets were finely powdered and an amount equivalent to 100 mg was weighed and transferred to 100 mL volumetric flask and 70 mL of methanol was added. The flask was shaken for ten min; finally, the volume was made up to mark with methanol and filtered through 0.45 µm Whatman filter paper. It was then suitably diluted and analysed using U.V. Spectrophotometer. (Schimadzu UV-1700) at 279 nm. The amount was calculated from calibration curve.

Swelling studies (Ganaprakash et al, 2010)

Formulated tablets were weighed individually (W0) and placed separately in a petri dish containing 50 mL of 0.1N HCl. The Petri dishes were placed in an incubator maintained at 37±0.5oC. The tablets were removed from the petri dish, at predefined intervals of time and reweighed (Wt), and the % swelling index was calculated using the following formula:

$$\% W_U = (Wt\text{-}Wo/Wo) \times 100$$

Where: WU – Water uptake, Wt – Weight of tablet at time t, Wo – Weight of tablet before immersion.

In vitro dissolution studies (Rosa et al., 1994)

The release of drugs (FAM, LAF and NIZA) from the prepared effervescent tablets was studied using USP-Type II paddle apparatus (Electrolab TDT 08L, dissolution tester, U.S.P.). Drug release profile was carried out in 900 mL of 0.1N HCl maintained at 37±0.5°C temperature at 100 rpm. 5 mL of samples were withdrawn at regular time intervals up to 12 h. The samples were replaced by equivalent volume of dissolution medium and were filtered through 0.45 µm Whatman filter paper. The samples were suitably diluted and analysed at 265.5 nm (FAM), 279 nm (LAF) and 314 nm (FAM) using (Shimadzu UV 1700) UV spectrophotometer.

Study of Drug Release Kinetics [43]

The drug release kinetics of Alfuzosin hydrochloride was determined by plotting the following kinetic models, using the data collected from in-vitro release studies. (Zero order, first order and Higuchi equations). The mechanism of Alfuzosin hydrochloride release from the tablets was determined by using Korsmeyer Peppas equations.

Zero-Order Kinetics:

Cumulative amount of drug released was plotted against time (C = K0t) where K0 is the zero-order rate constant expressed in units of concentration/time and t is the time in hours. A graph of concentration Vs time would yield a straight line with a slope equal to K0 and intercept the origin of the axis. This kinetics describes concentration independent drug release from the formulations. Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation:

$$Qt = Qo + Kot$$

Where, Qt = Amount of drug dissolved in time t, Qo = Initial amount of drug in the solution and, Ko = Zero order release constant.

First order kinetics:

First order as log cumulative percentage of drug remaining vs time. This kinetics describes concentration dependent drug release from the formulations. To study the first order release kinetics the release rate data were fitted to the following equation.

$$Log\ Qt = log\ Qo + K1t / 2.303$$

Where, Qt = Amount of drug released in time t, Qo = Initial amount of drug in the solution and K1 = First order release constant.

Higuchi Model:

Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semi-solid and/or solid matrixes. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. The Higuchi equation is

$$Qt = KH \times t1/2$$

Where, Qt = amount of drug released in time t and, KH = Higuchi dissolution constant. This model describes the release of drug on the basis of Fiskian diffusion as a square root of time dependent process from swellable matrix.

Korsmeyer Peppas Equations:

To evaluate the mechanism of drug release, the first 60% of drug release were plotted in Korsmeyer et al equation log cumulative percentage of drug released vs log time, and the exponent n was calculated through the slope of the straight line, $Mt / M\infty = Ktn$. Where $Mt/M\infty$ is the fractional solute release, t is the release time, K is a kinetic constant characteristic of the drug/polymer system, and n is an exponent that characterizes the mechanism of release of tracers. For cylindrical matrix tablets, if the exponent n = 0.45,

then the drug release mechanism is Fickian diffusion, and if 0.45 <n < 0.89, then it is non-Fickian or anomalous diffusion. An exponent value of 0.89 is indicative of Case-II Transport or typical zero-order release. To study this model, the release rate data is fitted to the following equation.

$$Mt / M = K. tn$$

Where, Mt / M = Fraction of drug release, K = Release constant, t = Drug release time and n = Diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form. The values of 'n' are, n = 0.45 Fickian (case I) release, 0.45 < n < 0.89 Non-Fickian (Anomalous) release, n = 0.89 Case II (Zero order) release, > 0.89 Super case II type release.

Hixson–Crowell Model:

To study the Hixson–Crowell model, the release rate data are fitted to the following equation.

$$Wo\ 1/3 - Wt\ 1/3 / Ks\ t$$

Where, Wo = Amount of drug in the pharmaceutical dosage form, Wt = Remaining amount of drug in the pharmaceutical dosage form, Ks = Constant incorporating the surface-volume relation.

RESULTS & DISCUSSION

Characterization of Drug

The drug sample obtained from Hetero Drugs Ltd (Hyderabad) was characterized by physical characters, micrometric characters, and analytical characters. Whereas results are discussed below:

Physical characterization

Physical characterization is the assurance of all the physical properties of a active pharmaceutical ingredient (API), for example, a melting point. The principal reason for performing physical portrayal is to comprehend and control drugs: When developing up another drug product need to ensure that it is steady during storage for a specific period (typically a few years). Therefore, it is applicable to recognize when presented to, for example, higher temperature or humidity. Physical characterization of drug including all organoleptic characters (colour, Odor, and appearance), melting point, and solubility were characterized and results are discussed below:

Organoleptic characteristics

Organoleptic properties are the aspects of creating experience via the senses including taste, smell, and touch. Cefdinir received was studied for organoleptic characteristics for example colour, Odor, and appearance. The results presented in table

Table No 4: Organoleptic characterization of drug

Sr. No	Identification test	Observed results	Reported standard
1	Colour	white to light yellow	white to light yellow
2	Odor	Odourless	Odourless
3	Appearance	Crystalline powder	Crystalline powder

Results of organoleptic characterization obtained confirmed that the obtained Cefdinir sample is pure; the results compared with reported standard results of the drug, which doesn't show any difference. The drug sample was white, observed by naked eyes, it was odourless confirmed by smelling with nose simply, and appeared to be a crystalline powder.

Melting point

An easily accessible M.P. physical parameter has significant potential for finding properties of the drug. M.P. is resolved in the capillary tube. The expression implies that the temperature where the substance is melted, as showed by the disappearance of solid, will be nearby ±4 °C from the expressed value, except if in any case demonstrated. Melting point (MP) of the drug by the capillary method in triplicate was performed, the average of these three determined, and results are mentioned in table.

Table No 5: The melting point of the drug

S. No	Observation	Melting point (Average)	Reported standard
1	170.25±1.35 ^{0}C	169.51±1.34 ^{0}C	168-170 ^{0}C
2	168.47±1.24 ^{0}C		
3	169.83±1.09 ^{0}C		

As a melting point study was performed in triplicate, the average of these three reads is considered as a final result of the melting point, which is compared with reported standard results, whereas no difference observed between them, it was 169.51±1.34 0C.

Solubility

It is the property of a chemical substance that may be solid, liquid, or gas known as solute to break down in a solvent. Any drug's solubility was tested in various solvents, results are determined in table.

Table No 6: The solubility of Cefdinir

S. No	Solvents/Buffers	Solubility (mg/mL)	Solubility
1	Water	8.83±5.69	Sparingly soluble
2	Ethanol	12.34±0.24	Sparingly soluble
3	Methanol	10.64±0.69	Sparingly soluble
4	Chloroform	8.96±0.13	Sparingly soluble
5	dichloromethane	1.06±0.002	Sparingly soluble
6	Phosphate buffer pH 1.2	0.75±1.87	Sparingly soluble
7	Phosphate buffer pH 6.8	17.85±0.95	Freely soluble

Solubility was checked in water, alcohol, and dichloromethane it showed good results as per standard solubility of the drug. The drug was soluble in water i.e. 8.83±5.69 mg/ml, sparingly soluble in alcohol i.e. 12.34±0.24 mg/ml, and in dichloromethane it showed 1.06±0.002 mg/ml that means practically insoluble.

Analytical characterization

This part of the characterization of the drug includes analytical parameters, determining absorption maxima in 0.1N HCl and water, and a calibration curve in both. This part also covers other analytical parameters like spectroscopy (FTIR) and loss on drying. All results of these parameters are listed below:

Determination of absorption maxima in Methanol

UV spectroscopy is about the spectroscopic absorption, adjoining noticeable spectral areas. This suggests it utilizes light in the noticeable and ranges nearby. The retention or reflectance in the range of visible straightforwardly influences the apparent shade of the synthetic compounds included. The λmax was determined in a methanol solution by producing a stock solution of 100 µg/ml, and running on UV spectra between 200 – 400 nm.

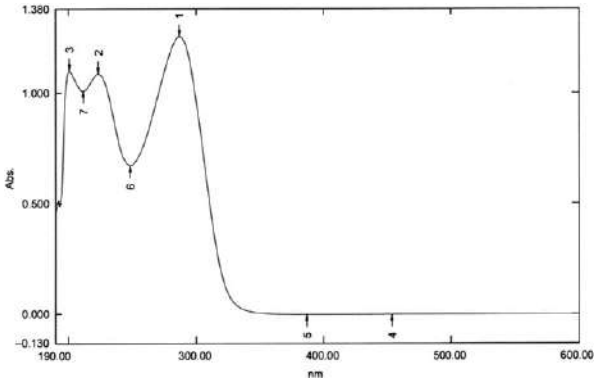

Figure 1: Absorption maxima of Cefdinir in Methanol

In the UV spectroscopy study, the maximum wavelength (λmax) of Cefdinir in methanol was 287 nm. The reported λmax of Cefdinir in methanol is 287 nm and the obtained graph is in figure.

Calibration curve of methanol in water

In analytical chemistry, a calibration curve, also known as a standard curve, is a general strategy for determining the concentration of a substance in an

unknown sample by contrasting the unknown with different standard samples of known concentration. The drug Cefdinir showed maximum absorption at 287 nm wavelength, thus considered as λmax of drug and calibration curve of the dilutions was run at this wavelength and the result is in figure.

Table 7: Absorption maxima of Cefdinir in methanol

S. No	Concentration (µg/mL)	Absorbance
1	0	0
2	2	0.198±0.02
3	4	0.301±0.06
4	6	0.527±0.08
5	8	0.716±0.07
6	10	0.906±0.05

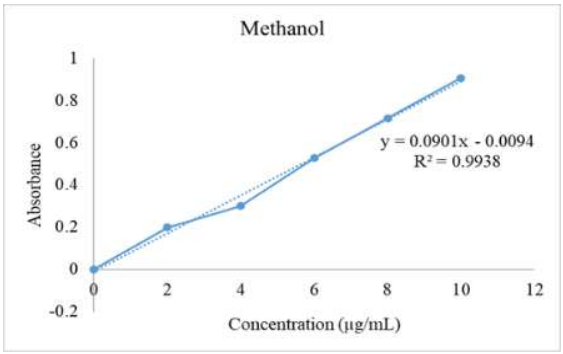

Figure 2 : Calibration curve of Cefdinir in Water (λmax-287 nm)

During the calibration curve of Cefdinir, the dilutions were made at 2, 4, 6, 8, and 10 and the correlation coefficient of 0.9938 was observed.

FTIR Spectroscopy

Cefdinir FTIR spectroscopy was performed on SHIMADZU 84005 spectrophotometer by manufacturing Cefdinir thin pellets with potassium bromide, and graph obtained as presented below:

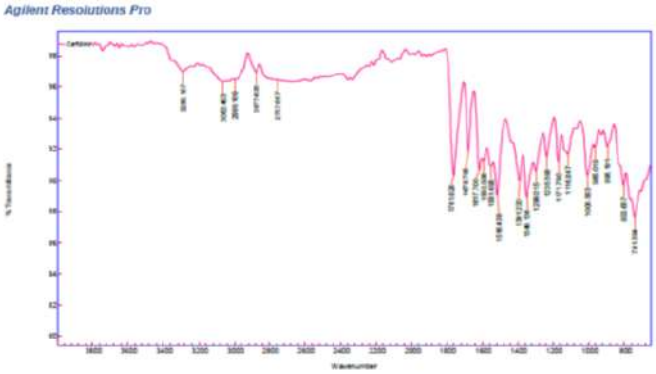

Figure 3 : FTIR spectrum of Pure drug (Cefdinir)

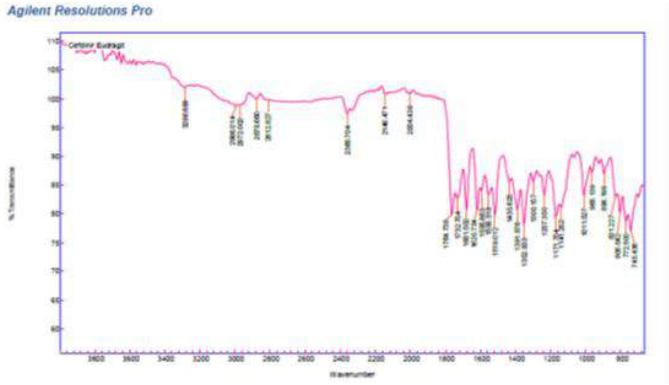

Figure 4 : FTIR spectrum of physical mixture

Compatibility studies were performed using FT-IR spectrophotometer. The spectra for pure drug and excipients are shown in figure and interpretation of spectra is reported. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. It does not show any major changes in peaks which indicate no well-defined interaction between Cefdinir and other excipients. This indicates that the drug is compatible with the formulation components. IR spectrum of cefdinir (Fig) is characterized by principal absorption peaks at 2,928 cm −1 (O–H stretch COOH), 2,849 cm −1 (C–H stretch cyclic), 1,761 cm −1 (C═O), 1,678 cm −1 (C═C alkene), 1,620 cm −1 (C═C aromatic), 1,516 cm −1 (N–H bending), 1,391 cm −1 (C–N stretch), and 656 cm −1 (C–S).

Pre-compressional and Formulation parameters

- The excipients and the drug cefdinir have no interactions (47).
- They showed their characteristic melting point profiles, cefdinir -melting point ≈ 168-170°C; Tartaric acid, fumaric acid, sodium bicarbonate, lactose and sucrose, ensuring their identity.
- The drug assay proved that the cefdinir supplied was of pharmacopeial standards.
- The solubility profile of the drug revealed, it is highly soluble in pH 6.8 buffer (47).
- The particle size determination of the drug, cefdinir confirmed that it can be used in a direct compression.

Micromeritic Studies

The cefdinir tablets were subjected to various micromeritic studies after formulation of cefdinir effervescent tablets. The results obtained are given below:

Bulk density

Bulk density is a derived property of powder which determines their packing property. The bulk density of powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another. The particle may pack in such a way as to leave large gaps between their surfaces, resulting in light powder or powder of low bulk density. On the other hand, the smaller particles may shift between the larger ones to form a heavy powder or one of high bulk density. The bulk density values less than 1.2 gm/cm3 indicates good flow characteristic property. Bulk density and tapped densities showed good packing ability of the powdered blend for compression process. Bulk and tapped densities of different formulations were calculated. In the present study, the bulk density values ranged between 0.432 to 0.451 gm/cm3 and 0.587±0.59 to 0.618±0.52.

Table 8: Micromeritic properties of cefdinir Tablets

F. Code	Bulk density (g/cm3)	Tapped density (g/cm3)	Angle of repose (θ)	Car's index (%)	Hausner's Ratio
F1	0.476±0.58	0.555±0.60	14.23±0.72	1.16±0.61	27.12±0.28
F2	0.487±0.69	0.587±0.59	17.03±0.63	1.20±0.63	28.16±0.30
F3	0.521±0.63	0.601±0.61	13.31±0.70	1.15±0.51	28.19±0.61
F4	0.499±0.75	0.592±0.57	15.70±0.62	1.18±0.55	25.64±0.52
F5	0.496±0.59	0.591±0.58	16.07±0.59	1.19±0.63	26.19±0.59
F6	0.501±0.72	0.602±0.61	16.61±0.60	1.20±0.59	26.20±0.48
F7	0.512±0.60	0.600±0.53	14.66±0.63	1.17±0.65	29.20±0.64
F8	0.515±0.64	0.612±0.62	15.84±0.64	1.18±0.58	28.16±0.59
F9	0.510±0.65	0.609±0.57	16.25±0.69	1.19±0.65	27.82±0.52
F10	0.499±0.59	0.598±0.63	16.55±0.58	1.19±0.62	26.47±0.55
F11	0.498±0.65	0.597±0.49	16.58±0.61	1.19±0.59	25.97±0.68
F12	0.500±0.62	0.594±0.50	15.81±0.54	1.18±0.54	26.74±0.70
F13	0.512±0.59	0.618±0.52	17.15±0.57	1.20±0.49	28.19±0.72
F14	0.500±0.60	0.601±0.53	16.80±0.59	1.20±0.56	27.90±0.78
F15	0.499±0.63	0.597±0.57	16.41±0.63	1.19±0.55	26.08±0.81
F16	0.489±0.59	0.598±0.62	18.22±0.51	1.22±0.26	26.15±0.85
F17	0.490±0.61	0.596±0.64	17.78±0.50	1.21±0.28	27.34±0.59

The results of all formulations F1 to F17 of cefdinir tablets are shown in Table, which were evaluated for variable parameters such as bulk density, tapped density, % Compressibility index, Hausner's ratio and angle of repose. The % Compressibility index was in the range of 25.64±0.52 to 29.20±0.64 for all the formulations F1 to F17 indicating good flow property. The values of angle of repose for formulations F1 to F17 was found to be in the range of 25-30 which indicated the good flow potential.

Angle of repose

Flow property of a powder was assessed by determining angle of repose of the powders. The angle of repose is high if the cohesive and other forces are high. The angle of repose between 350 and 450 indicates the powder does not have satisfactory flow property. The angle of repose around 25° indicates very good flow property. In the present study, the angle of repose values of the prepared tablets ranged between 27.95±0.42 to 36.84±0.16 (Table no).

Hausner's ratio

The Hausner ratio values less than 1.259±0.15 indicate good flow characteristic property. In the present study, the Hausner's value ranged from 1.194±0.01 to 1.365±0.03 (Table no).

Formulation of cefdinir Effervescent tablets

All the tablets were prepared by effervescent approach. The concentration of all the three selected semi-synthetic polymers was decided on trial-and-error basis. Sodium bicarbonate, tartaric acid and fumaric acid in the ratio of 1:0.5, were incorporated as a gas-generating agents based on earlier studies (Salve, 2011). PVPK 30 (5%) and MCC (14.4%–44.4%) were used as binder and diluent respectively. Talc (1%) was used as lubricant and magnesium stearate (2%) was employed as glidant to improve the flow of the powder. FTIR study showed that all the polymers used were compatible with cefdinir. From the earlier literature it was evident that sodium bicarbonate and tartaric acid is a good polymer for drug delivery system as it is a matrix forming and low-density polymer (Lakshmaiah et al., 2014).

Experimental Design:

Results of experimental design batches (F1 to F17) were shown in table. Box-Behnken design was used to optimize the amount of sodium bicarbonate, tartaric acid and fumaric acid to get the faster disintegration time and higher amount of swelling index and drug release after 5 min. The results of statistical analysis for design batches were obtained by Design Expert® software and were shown in table. The polynomial equation generated for each response by software was described in equation 1-3 and response surface plot for each response was shown in figure.

Table 9: Experiment design of cefdinir effervescent tablets

Std	Run	X1	X2	X3	Y1	Y2	Y3
1	6	50	20	40	12±2	89.61±0.2	186±18
2	17	100	20	40	19±3	75.42±0.4	198±11
3	13	50	40	40	12±1	95.02±0.3	236±12
4	8	100	40	40	22±5	68.42±0.1	136±17
5	16	50	30	30	15±4	82.19±0.5	210±15
6	4	100	30	30	16±2	86.95±0.6	216±16
7	14	50	30	50	16±1	84.13±0.8	221±14
8	1	100	30	50	32±6	46.35±0.9	106±12
9	12	75	20	30	12±2	94.82±0.7	227±13
10	11	75	40	30	27±1	72.15±0.1	134±14
11	2	75	20	50	31±5	59.84±0.5	118±10
12	3	75	40	50	25±3	76.82±0.3	164±12
13	15	75	30	40	17±4	84.15±0.4	185±14
14	9	75	30	40	16±5	86.42±0.1	192±16
15	10	75	30	40	22±1	78.46±0.6	187±12
16	5	75	30	40	15±2	83.19±0.5	195±15
17	7	75	30	40	18±5	85.07±0.3	188±13

Effect of Disintegration Time

The disintegration time was found in a range of 12±1 sec to 32±6 sec for all the formulations.

The Model F-value of 14.02 implies the model is significant. There is only a 0.11% chance that an F-value this large could occur due to noise. P-values less

than 0.0500 indicate model terms are significant. In this case A, C, AC, BC, A^2, C^2 are significant model terms. The Lack of Fit F-value of 0.21 implies the Lack of Fit is not significant relative to the pure error. There is an 88.78% chance that a Lack of Fit F-value this large could occur due to noise. The Predicted R^2 of 0.8165 is in reasonable agreement with the Adjusted R^2 of 0.8798; i.e. the difference is less than 0.2. Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 12.330 indicates an adequate signal.

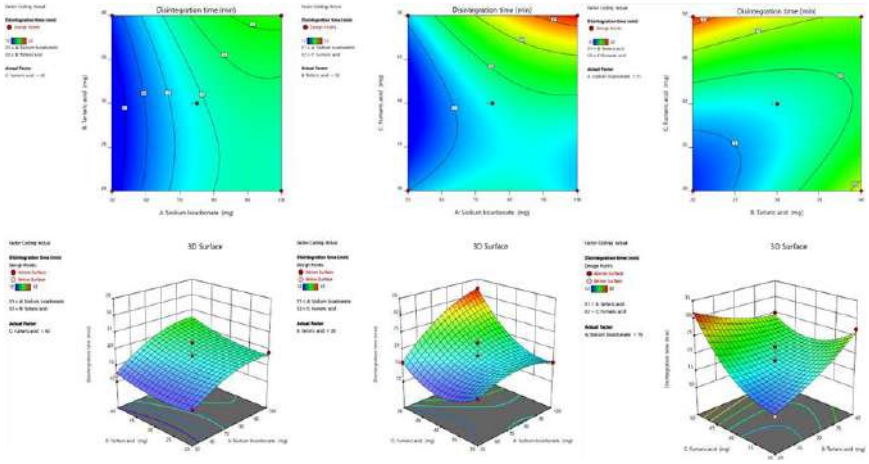

Figure 5. Counter and response 3D Surface Plot for Disintegration Time

ANOVA for Quadratic Model

Table 10. Response Y1: Disintegration Time

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	607.36	9	67.48	14.02	0.0011	significant
A	144.50	1	144.50	30.01	0.0009	
B	18.00	1	18.00	3.74	0.0944	
C	144.50	1	144.50	30.01	0.0009	
AB	2.25	1	2.25	0.4674	0.5162	
AC	56.25	1	56.25	11.68	0.0112	
BC	110.25	1	110.25	22.90	0.0020	
A^2	30.13	1	30.13	6.26	0.0409	
B^2	7.39	1	7.39	1.54	0.2552	
C^2	98.02	1	98.02	20.36	0.0028	
Residual	33.70	7	4.81			
Lack of Fit	4.50	3	1.50	0.2055	0.8878	not significant
Pure Error	29.20	4	7.30			
Cor Total	641.06	16				

Drug Release after 5 min

Drug release after 5 min was obtained from 46.35±0.9% to 95.02±0.3 % for all the formulations F1 to F17.Drug release after 5 min = +83.46 -9.23A -0.9100B -8.62C -3.10AB -10.64AC +9.91BC -1.17A2 -0.1690B2 -7.38 C2 The Model F-value of 33.88 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case A, C, AC, BC, C^2 are significant model terms. The Lack of Fit F-value of 0.66 implies the Lack of Fit is not significant relative to the pure error. There is a 61.66% chance that a Lack of Fit F-value this large could occur due to noise. The Predicted R^2 of 0.8573 is in reasonable agreement with the Adjusted R^2 of 0.9487; i.e. the difference is less than 0.2. Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 22.704 indicates an adequate signal.

ANOVA for Quadratic Model

Table 11: Response Y2: Drug release after 5 min

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	2407.62	9	267.51	33.88	< 0.0001	significant
A	680.99	1	680.99	86.25	< 0.0001	
B	6.62	1	6.62	0.8391	0.3901	
C	594.61	1	594.61	75.31	< 0.0001	
AB	38.50	1	38.50	4.88	0.0630	
AC	452.41	1	452.41	57.30	0.0001	
BC	393.03	1	393.03	49.78	0.0002	
A^2	5.78	1	5.78	0.7319	0.4206	
B^2	0.1203	1	0.1203	0.0152	0.9052	
C^2	229.42	1	229.42	29.06	0.0010	
Residual	55.27	7	7.90			
Lack of Fit	18.36	3	6.12	0.6635	0.6166	not significant
Pure Error	36.90	4	9.23			
Cor Total	2462.88	16				

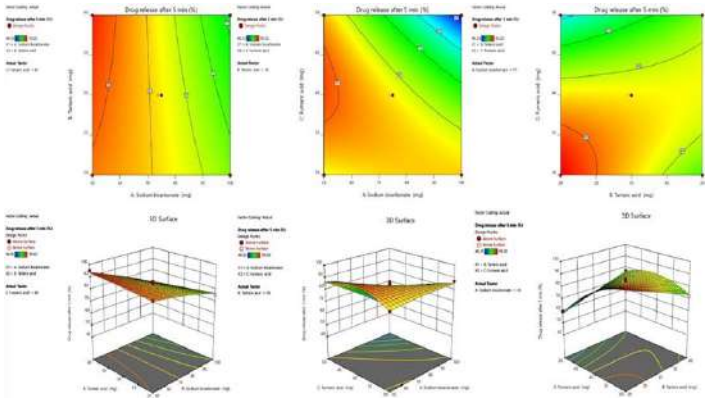

Figure 6 : Counter and response 3D Surface Plot for Drug Release after 5 Min

Swelling index studies

The swelling index was found in a range of 106±12 to 236±12 for all the formulations.

Swelling index = +189.40 -24.63A -7.38B -22.25C -28.00AB -30.25AC +34.75BC +13.55A2 -13.95B2 -14.70C2The Model F-value of 56.04 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case A, B, C, AB, AC, BC, A^2, B^2, C^2 are significant model terms. The Lack of Fit F-value of 5.28 implies there is a 7.09% chance that a Lack of Fit F-value this large could occur due to noise. The Predicted R^2 of 0.8208 is in reasonable agreement with the Adjusted R^2 of 0.9687; i.e. the difference is less than 0.2. Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 23.617 indicates an adequate signal.

ANOVA for Quadratic model.

Table 12: Response Y3: Swelling index

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	23304.08	9	2589.34	56.04	< 0.0001	significant
A	4851.13	1	4851.13	104.99	< 0.0001	
B	435.13	1	435.13	9.42	0.0181	
C	3960.50	1	3960.50	85.71	< 0.0001	
AB	3136.00	1	3136.00	67.87	< 0.0001	
AC	3660.25	1	3660.25	79.21	< 0.0001	
BC	4830.25	1	4830.25	104.53	< 0.0001	
A^2	773.06	1	773.06	16.73	0.0046	
B^2	819.38	1	819.38	17.73	0.0040	

C^2	909.85	1	909.85	19.69	0.0030	
Residual	323.45	7	46.21			
Lack of Fit	258.25	3	86.08	5.28	0.0709	not significant
Pure Error	65.20	4	16.30			
Cor Total	23627.53	16				

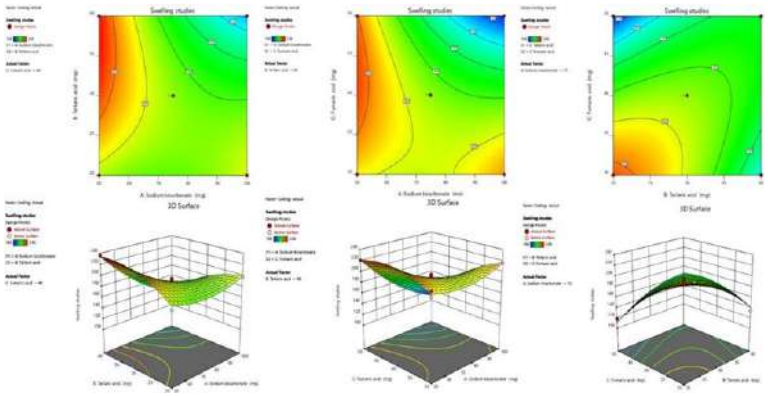

Figure 7: Counter and response 3D Surface Plot for swelling index

Post -compression physicochemical evaluation of cefdinir effervescent tablets

The formulated effervescent tablets were subjected for post compressional evaluation such as visual inspection, hardness, weight variation, friability, uniformity of drug content, in vitro buoyancy, swelling, in vitro dissolution, stability and similarity studies. The results are summarized in Table.

Table 15: Post compression parameters

F. no	Weight variation	Hardness (Kg/cm^2)	Friability (%)	Thickness (mm)	Drug content (%)
F1	600±0.50	4.5±0.48	0.29±0.85	4.01±0.32	95.10±0.75
F2	598±0.39	4.8±0.52	0.35±0.78	4.11±0.42	89.50±0.82
F3	599±0.52	4.9±0.47	0.28±0.79	4.21±0.38	91.20±0.56
F4	600±0.43	5.1±0.44	0.31±0.82	4.18±0.53	93.15±0.71
F5	598±0.58	5.2±0.52	0.28±0.83	4.45±0.83	94.20±0.58
F6	600±0.32	4.9±0.49	0.29±0.85	4.19±0.53	92.19±0.53
F7	599±0.39	5.0±0.53	0.30±0.79	4.12±0.55	89.50±0.63
F8	600±0.41	5.1±0.49	0.28±0.78	4.19±0.63	98.85±0.65
F9	599±0.53	5.0±0.52	0.21±0.81	4.20±0.72	97.10±0.71
F10	597±0.48	4.9±0.40	0.22±0.80	4.16±0.68	89.53±0.68
F11	598±0.52	5.0±0.48	0.30±0.77	4.09±0.29	96.30±0.73
F12	600±0.53	4.9±0.53	0.32±0.75	4.20±0.40	91.34±0.69
F13	601±0.48	5.0±0.50	0.40±0.70	4.21±0.52	96.90±0.70
F14	602±0.50	4.8±0.49	0.39±0.91	4.17±0.63	92.21±0.82
F15	599±0.53	4.9±0.47	0.39±0.92	4.19±0.42	93.60±0.78
F16	600±0.58	5.0±0.53	0.41±0.86	4.20±0.49	97.80±0.68
F17	598±0.62	5.1±0.55	0.45±0.82	4.14±0.56	94.40±0.60

Visual inspection

The prepared tablets were inspected visually for general tablet deformities. The tablets were smooth with uniform in size, shape and colour. There was no lamination or chipping was observed in all the tablets which indicated that the tablet-instrumentation was compatible with the powder blends and resulting in good tablet characteristics.

Hardness

The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness. Hardness in the prepared tablets was found to be in the range of 4.5±0.48–5.2±0.52 kg/cm2. Hardness of

the tablets was found to increase with an increasing in polymer concentration. Similar pattern of results was observed in the study done by Chauhan et al, (2010).

Weight variation

The weight variation of prepared formulations was found in the range of 597±0.48 –602±0.50 mg. All the batches of tablets were found to pass the weight variation test. The percentage deviation of the individual tablet weights from the average tablet weight was found to be within the I.P. limits of ±7.5 %.

Friability test

The friability loss of prepared tablets was found to be between 0.21±0.81% and 0.45±0.82% when tested using Roche friabilator. All batches of tablets passed the test and were within the limits of less than 1% which indicated that the tablets were mechanically stable.

Drug content uniformity

The drug content uniformity of the prepared tablets was examined as per I.P. specification and was found compliant. The drug content of the formulations was in the range 89.50±0.63% to 98.85±0.65% showing the uniformity of drug distribution in the prepared tablets. (Parija, 2013). None of the individual drug content values were outside the average content values of 90% to 110% as per IP.

Swelling index

Results of water uptake study showed that the order of swelling in these polymers could Indicate the rates at which the preparations are able to absorb water and swell. Maximum Liquid uptake and swelling of polymer was achieved up to 8 hrs and then gradually Decreased due to erosion. The complete swelling was achieved by the end of 8 hrs. The % of swelling of F7 was Higher due to increase in the concentration of polymer which also gives the firm structure to the tablet form.

Stability studies

Stability studies were performed as ICH guidelines on formulation F8. Samples were analysed after storage for 0, 1, 2,3, 6, 9 and 12 months and evaluated for appearance, hardness, drug content and drug release studies as described in 3.9 and results are given in tables. All the tested parameters found to be with in the acceptable limits, the range for drug content is 94.38±0.38 to 98.85±0.65%.

Table 13: Stability studies of optimized formulation

Stability chamber	Time	Appearance	Drug content
40º C ± 2º C / 75% RH	Initial	Brownish colour	98.85±0.65
	1 Month	No change	98.82±0.62
	2Months	No change	97.78±0.53
	3Months	No change	96.52±0.40
	6 Months	No change	95.48±0.43
25º C ± 2º C / 60% RH ± 5% RH	Initial	No change	98.85±0.65
	1 Month	No change	97.75±0.58
	2Months	No change	96.58±0.45
	3Months	No change	95.47±0.40
	6Months	No change	94.38±0.38

Invitro drug release studies

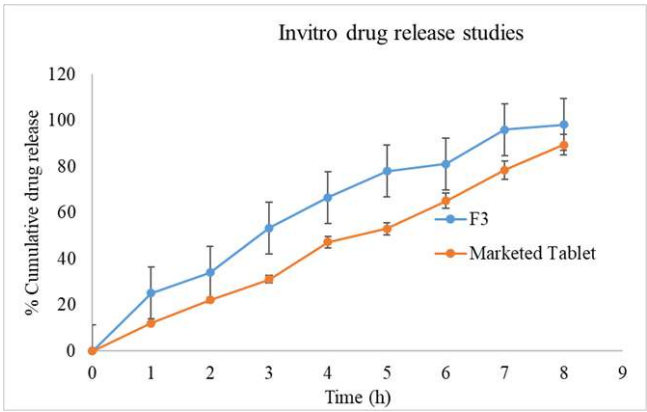

Figure 8 : Drug release studies of Optimized and marketed formulation

Table 14: Evaluation of drug release studies

Time	F3	Marketed Tablet
0	0	0
1	25.23±0.32	12.10±0.29
2	34.08±0.29	22.19±0.27
3	53.43±0.28	31.20±0.31
4	66.62±0.31	47.25±0.30
5	78.1 ±0.32	53.10±0.33
6	81.16±0.28	65.12±0.21
7	96.10±0.30	78.49±0.42
8	98.18±0.32	89.36±0.31

Cefdinir release was found to decrease with an increase in polymer concentration. Drug release was maximum (100±0.12%) for formulation FS4 which was constituted with low viscosity acids. The increased density of polymer at higher concentration results in an increased diffusional pathlength, which leads to an overall decrease in release of the drug. Although composition of tartaric acid and fumaric acid sustains the drug release for a longer period of time up to 8 h, this controlled release of drug from F3 could be attributed to the formation of a thick gel structure that delays the drug release from the tablet matrix.

Drug release kinetic studies

The mechanism of drug release for the above formulations was determined by calculating the correlation coefficient (R2value) for the kinetic models, viz., zero-order, first-order, Higuchi, and Korsmeyer–Peppas corresponding to the release data of each formulation. The results of the kinetic models are summarized in Tables. For most of the formulations the R2 value of Korsmeyer–Peppas and zero-order model was nearer to one than those of other kinetic models. Thus, it could be drawn from the results that the drug release follows zero-order and Korsmeyer–Peppas model mechanisms.The 'n' values of Korsmeyer–Peppas model for the best formulations were in the range of 0.45–0.85. Therefore, the most probable mechanism of release was found to be non-Fickian diffusion or anomalous diffusion for the formulations tested. The time required for dissolution of 50% (T50) and 90% (T90) were determined. The results of drug release kinetics are shown in Table.

Table 15: Drug Release Kinetics of Formulation F3

TIME	%CDR	SQARE T	LOG T	LOG%CDR	ARA	LOG%ARA
0	0	0	0	0	0	0
1	25.23	1	0	1.401917	74.77	1.873727
2	34.08	1.414214	0.30103	1.5325	65.92	1.819017
3	53.43	1.732051	0.477121	1.727785	46.57	1.668106
4	66.62	2	0.60206	1.823605	33.38	1.523486
5	78.1	2.236068	0.69897	1.892651	21.9	1.340444
6	81.16	2.44949	0.778151	1.909342	18.84	1.275081
7	96.10	2.645751	0.845098	1.982723	3.9	0.591065
8	98.18	2.828427	0.90309	1.992023	1.82	0.260071

SUMMARY & CONCLUSION

The drug cefdinir are used as antibiotics. Preformulation studies has been carried out on various parameters such as Physical appearances, Solubility Studies, Melting point determination, Drug polymer compatibility studies and construction of calibration graph for three drugs separately. The preformulation studies confirmed that the three drugs were of experimental quality as per the specifications. FTIR and DSC showed no momentous interaction among them and conclude that the selected components were incredibly appropriate for the formulation. Calibration curve was noticed linear which denotes that the used wavelength 290 nm for cefdinir and 287 nm. In this study same proportion of natural and synthetic polymers and other excipients were used for preparation of cefdinir effervescent tablets. From the study, it is was increased, with increasing polymer and by the usage of Xanthum gum which has higher effervescent for cefdinir. Drug release is a key factor

to evaluate the stability of effervescent tablets for cefdinir cefixime effervescent tablets. Effervescent tablets of cefdinir were prepared using the different acid sources like citric acid, tartaric acid, fumaric acid and carbonate sources like sodium carbonate, sodium bicarbonate,potassium bicarbonate.The concentration of acid and carbonate sources was also changed during the study. After that study, sodium bicarbonate was selected as carbonate source. Trial was also been taken for combination of acid to reduce disintegration time. The combination of tartaric acid and fumaric acid gave fast disintegration. Further optimization was done using box Behnken design. The study concluded that the combination of sodium bicarbonate, tartaric acid and fumaric acid approach for development of effervescent tablet aids to achieve faster disintegration and faster drug release property for cefdinir. The Box-Behnken design was employed for the optimization and the effect of process parameters and their interaction on the effervescent formulation were studied. The *invitro* drug release of most of the formulations of cefdinir effervescent tablets shown zero order kinetic pattern of drug release which is confirmed by the correlation coefficient value nearer to linearity. Followed by *invitro* drug release studies, the drug release values of cefdinir, effervescent tablets has been fitted to various other kinetics models such as Higuchi, Peppas plots. The *in-vitro* release plots of all the formulations of cefdinir, effervescent tablets were suggestive of zero order release and are diffusion mediated which was demonstrated from the regression value Higuchi's plot.

REFERENCE

1. Alexander S, Juergen S, Bodmeier R. Gastroretentive drug delivery systems Expert Opin. Drug Delivery. 3(2), 2006, 217-233.
2. Hirtz J. The GIT absorption of drugs in man: A review of current concepts and methods of investigation. Br J Clin Pharmacol. 19, 1985, 77S-83S.
3. Ponchel G, Irache JM. Specific and non-specific bioadhesive particulate system for oral delivery to the gastrointestinal tract. Adv Drug Del Rev. 34, 1998, 191- 219.
4. Vantrappen G R, Peeters T L, Janssens J. The secretory component of interdigestive migratory motor complex in man, Scand J Gastroenterol. 14, 1979, 663-667.
5. Pooja Mathur, Kamal Saroha, et al., Effervescent drug delivery system: An innovative acceptable approach in gastroretentive drug delivery, Archives of Applied Science Research, 2 (2), 2010, 257-270.
6. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. Pharm Res. 14, 1997, 815-819.
7. Rednick AB, Tucker SJ. Sustained release bolus for animal husbandry. US patent 3 507 952. April 22, 1970.
8. Park HM, Chernish SM, Rosenek BD, et al. Gastric emptying of enteric-coated tablets. Dig Dis Sci 29, 1984, 207-12.
9. Groning R, Heun G. Dosage forms with controlled gastrointestinal passage— studies on the absorption of nitrofurantoin. Int J Pharm. 56, 1989, 111-116.
10. Standley S. Davis. Formulation strategies for absorption window. DDT. 10(4), 2005, 249-257.
11. P.R. Sheth, J.L. Tossounian, Sustained release pharmaceutical capsules, US Patent 4, November 21, 1978, 126, 672.
12. Hoffman A and Strepensky D. Pharmacodynamic aspects of modes of drug administration for optimization of drug therapy, Crit Rev Ther Drug Carrier Syst, 16, 1999, 571-639.
13. Stockwell AF, Davis SS, walker SE. In vitro evaluation of alginate gel system as sustained release drug delivery system. J Control Release. 3, 1986, 167-175.
14. Hejazi R and Amiji M. Stomach specific anti H. pylori therapy. I: preparation and characterization of tetracycline of a effervescent multiple-unit capsule, a high-density loaded chitosan microsphere, Int J Pharm, 235, 2002, 87-94.
15. Dave BS, Amin AF and Patel M. Gastroretentive drug delivery system of Ranitidine HCl formulation and In vitro evaluation. AAPS Pharm Sci Tech, 5, 2004, 1-10.
16. Alexander S, Juergen S, Bodmeier R. Gastroretentive drug delivery systems Expert Opin. Drug Delivery. 3(2), 2006, 217-233.
17. Hirtz J. The GIT absorption of drugs in man: A review of current concepts and methods of

investigation. Br J Clin Pharmacol. 19, 1985, 77S-83S.
18. Ponchel G, Irache JM. Specific and non-specific bioadhesive particulate system for oral delivery to the gastrointestinal tract. Adv Drug Del Rev. 34, 1998, 191- 219.
19. Vantrappen G R, Peeters T L, Janssens J. The secretory component of interdigestive migratory motor complex in man, Scand J Gastroenterol. 14, 1979, 663-667.
20. Pooja Mathur, Kamal Saroha, et al., Effervescent drug delivery system: An innovative acceptable approach in gastroretentive drug delivery, Archives of Applied Science Research, 2 (2), 2010, 257-270.
21. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. Pharm Res. 14, 1997, 815-819.
22. Rednick AB, Tucker SJ. Sustained release bolus for animal husbandry. US patent 3 507 952. April 22, 1970.
23. Park HM, Chernish SM, Rosenek BD, et al. Gastric emptying of enteric-coated tablets. Dig Dis Sci 29, 1984, 207-12

HOW TO CITE: Sudarshan Mirgal*, Dr. Bharat Tekade, Dr. Mohan Kale, Formulation and Optimization of Effervescent Tablets by Design Of Experiments, Int. J. Sci. R. Tech., 2025, 2 (1), 218-235. https://doi.org/10.5281/zenodo.14650499