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Formulation and evaluation of inclusion complex Tablet of Furazolidone

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Abstract

Furazolidone is a nitro furan antimicrobial agent used in the treatment of diarrhea or enteritis caused by bacteria or protozoan infections. Furazolidone is also active in treating typhoid fever, cholera and salmonella infections. In present research work an attempt has been made to prepare inclusion complex tablets of Furazolidone with increased rate of dissolution may leads to increase bioavailability. Formulation of inclusion complex tablet of poorly soluble Furazolidone by β Cyclodextrin and Hydroxypropyl β cyclodextrin by different ratio (1:1), (1:2), (1:3) using kneading method. The papered inclusion complex evaluated by phase solubility study optimized inclusion complex Furazolidone: Hydroxypropyl β Cyclodextrin (1:2) ratio give enhanced solubility. After optimization of inclusion complex of Furazolidone: Hydroxypropyl β Cyclodextrin inclusion complex were prepared by direct compression method. Sodium starches Glycolate, croscarmellose sodium, crospovidone are used as a superdisintegrants.

Drug polymer interactions were investigated using Fourier transform infrared spectroscopy. The prepared formulation were evaluated for various parameters like weight variation, hardness, friability, drug content, disintegration time, wetting time, in vitro drug release, Batch D5was optimized formulation containing 5% Crospovidone showed less disintegration time 20 sec and more than 99.54% drug release at 30 mint. Stability studies were carried out at 40 ± 2°C /75 ± 5% RH for formulation D5 for 1 month Stability studies on the best formulation indicated that there was no significant change found in hardness, disintegration time, wetting time and drug release of tablets.

Key words: Inclusion Complex, Furazolidone, Solubility, Bioavailability, β-Cyclodextrin, Superdisintegrants

Introduction

Solubility is the property of a solid, liquid, or else gaseous chemical material called solute to dissolve in a solid, liquid, or else gaseous solvent to create a homogeneous solution of the solute within the solvent. The solubility of a material mainly depends on the solvent use as well as on temperature plus pressure. The amount of solubility of a substance in a specific solvent is considered as the saturation concentration where addition more solute does not enhance its concentration in the solution.

The solvent is usually a liquid, which can be a unpolluted material or a combination of two liquids. One may besides speak of solid solution, but rarely of solution in a gas. The extent of solubility range generally from infinitely soluble (fully miscible) solvent such as ethanol in water, to poorly soluble, such as silver chloride in water. The word insoluble is often applied to poorly or very poorly soluble compounds**.**

Solubility occurs underneath dynamic equilibrium, which means that solubility outcome from the simultaneous and opposing process of dissolution and phase joining (e.g., precipitation of solid). Solubility equilibrium occurs when the two processes proceed at a constant rate. Underneath certain conditions equilibrium solubility may be there exceeded to give a so-call supersaturated solution, which is metastable.[1-4]

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Importance of Solubility

Oral ingestion is the mainly convenient and commonly employed route of remedy delivery due to its ease of administration, highest patient compliance, cost efficiency, least sterility constraint, and flexibility in the design of dosage type As a result, many of the generic medicine companies are inclined more to manufacture bioequivalent oral drug products .

However, the main challenge with the design of oral dose forms lies with their poor bioavailability**.** The oral bioavailability depends on several factors include aqueous solubility, drug permeability, dissolution rate, first-pass metabolism, Presystemic metabolism, and susceptibility to efflux mechanisms. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability.

Technique for Solubility Enhancement [4-5]

Physical Modifications

Particle size reduction similar to micronization and nanosuspension, modification of the crystal habit like to polymorphs, amorphous form and co crystallization, drug diffusion in carrier like eutectic mixtures, solid dispersions, solid solution and cryogenic technique.

Chemical Modifications

Change of PH, use of buffer, derivation, complexation, and salt creation. Supercritical fluid process, make use of adjuvant like surfactant, solubilizers, co solvency, hydro trophy, and novel excipients.

Cyclodextrins

Cyclodextrins were discovered approximately 100 years ago with the foundation of Cyclodextrins chemistry being laid down in the first half of this century. In the beginning only small amounts of relatively impure Cyclodextrins could be generated and high production costs prevented their industrial usage. Recent bio-technological advancements have resulted in dramatic improvements in the efficiency of manufacture of Cyclodextrins, lowering the cost of these materials and making highly purified Cyclodextrins and Cyclodextrins derivatives available.

Pharmaceutical applications of Cyclodextrins as additive and drug complexing agents have been rapidly growing. The interaction of guest molecules with Cyclodextrins may induce useful modifications of the chemical and physical properties of the guest molecules, which may lead to improve stability, solubility in aqueous medium and bio-availability. Poorly water soluble drugs therefore can be orally administered in the complexes form by taking advantage of the well established low toxicity of the Cyclodextrins by the oral route. Cyclodextrins appears to be the most useful complexing agent because of its unique cavity size, and ease with which it can be obtained on the industrial scale leading to reasonably cheaper price of the compound.

Solubility Enhancement by Inclusion Complex Formation [6-7]

Solubility is an essential parameter which may affect the drug dissolution and absorption behavior. For orally administered medicine solubility is one of the rates limiting parameter to get their concentration in systemic circulation.

The poor dissolution characteristics of relatively insoluble drugs have long been a difficulty to Pharmaceutical Industry. A number of modern drugs are weakly soluble in water & aqueous fluids. Their absorption and bioavailability require improvement in dissolution rate and efficiency. Among various methods for improving the dissolution rate and bioavailability, cyclodextrin complexation was found to be especially successful with a number, of poorly soluble drugs such as Rofecoxib, Nimesulide, Ciprofloxacin, Tolbutamide, Paracetamol, Diclofenac sodium etc. Cyclodextrins such HP-β cyclodextrin, γ-cyclodextrin, α, β, hydroxyl propyl-β-cyclodextrin, α-cyclodextrin, Triacetyl-β-cyclodextrin , Methylated-β cyclodextrin , Hydroxy ethyl-β-cyclodextrin etc., are used for preparing cyclodextrin complexes.

They require enhancement in solubility and dissolution rate for improving their oral bioavailability. In the present investigation study were carried out on cyclodextrin complexes of Furazolidone for increase the dissolution rate. Furazolidone is a nitro furan antimicrobial agent use in the treatment of diarrhea or enteritis caused by bacteria or protozoan infection. Furazolidone is too active in treating typhoid fever, cholera and salmonella infections.

Material and Methods

Materials: Furazolidone, crospovidone (Superdisintegrants) was gifted from Modern laboratory Indore .β cyclodextrin was purchased from Otto Biochemical. Crospovidone, Cross Carmellose Sodium, and Sodium Starch Glycolate was gifted from modern laboratory Indore.

Spectrophotometric Estimation Furazolidone [8]

Calibration curve of Furazolidone

Measurement of spectra of Furazolidone by using UV visible 1600 Shimadzu double beam Spectrophotometer and solvent was ethanol that was used for measuring absorbance.

a) Wavelength selection

Absorbance was observed at 259 nm.

b) Standard stock solution

For standard stock solutions (1000ug/ml), perfectly weighed 100 mg of Furazolidone be taken or transfer to a volumetric flask or sufficient ethanol be added to generate 100 ml

c) Dilutions preparation

From the standard stock solution of Furazolidone , different dilution be prepared .seven different dilutions of 2 ug/ml, 4ug/ml, 6ug/ml, 8ug/ml, 10ug/ml. were prepare .1000ug/ml standard stock solution .

d) Procedure

Following preparation of standard or sample solution ,measurement of the absorbance of different dilution (2ug/ml, 4ug/ml, 6ug/ml, 8ug/ml, 10ug/ml,) inside 1cm. cuvette via use UV-visible spectrophotometer on the wavelength of maximum absorbance 259 nm, use the blank solution be performed.

Drug –Excipient Compatibility Study [9-11]

Fourier Transform Infrared (FTIR) Spectroscopic Analysis

FT-IR Spectroscopy was conducted using a FTIR spectrometer (FTIRss1700, Shimadzu, Kyoto, Japan) and the spectra were recorded in the wavelength region of 4000 Impact factor: 0.3397/ICV: 4.10 176Krupa et al. / Pharma Science Monitor 6(2), Apr-Jun 2015, 174-195 400 cm 1. The procedure consisted of dispersing the samples in KBr and gentle grinding to Prepare pellets.

Method of Formation of Inclusion Complex

Kneading method-Furazolidone with β-cyclodextrin and HP β-cyclodextrin were triturated in a pestle mortar with a small volume of a solvent blend of water-methanol (1:1). The thick slurry was kneaded for 45 mints and then dried at 55 ^{o} C until dry. The dried mass was pulverized and sieved through mesh No.60.

Physical mixture- Furazolidone with beta cyclodextrin and HP β-cyclodextrin were mixed in a mortar for about one hour with constant trituration, passed through sieve no.100 and store in a desiccator over fused calcium chloride.

Preliminary study for selection of complex

Table 1: Preliminary study for selection of complex

Batch code	Composition	Molar ratio
C1	Furazolidone + β cyclodextrin	1:1
C2	Furazolidone + β cyclodextrin	1:2
C3	Furazolidone + β cyclodextrin	1:3
C4	Furazolidone + H P β Cyclodextrin	1:1
C5	Furazolidone + H P β Cyclodextrin	1:2
C6	Furazolidone + H P β Cyclodextrin	1:3

Drug – Excipients interaction study

Physical observation of sample was done visually at every week for any change in the sample mixture for 4 weeks.

Discoloration

For discoloration study, drug was mixed with all the excipients and observed for any discoloration for 4 weeks.

Interaction

The compatibility of drug and various excipients was studied by Thin Layer Chromatography (TLC) technique. For study purpose, Furazolidone 10 mg was mixed thoroughly by mortar and pestle with excipient in ratio of 1:5 respectively and placed in tightly closed glass vials.

All the vials were kept at 40^{0}C for 4 weeks. The sample was analyzed by physical observation and thin layer chromatography before and after storage.

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Evaluation of Furazolidone Cyclodextrin Complex [12-15]

Solubility study: Solubility study of Furazolidone inclusion complex in phosphate buffer ph 6.8 carried out by adding excess amount of Furazolidone, Furazolidone: -β cyclodextrin, Furazolidone:HP-β Cyclodextrin in different ratio(1:1,1:2,1:3) were placed into 25 ml phosphate buffer ph 6.8 different glass flask containing. And flask closed with stopper. The content of flask was equilibrated by shaking for 24 hours in thermostatically controlled water bath at 250C. After attainment of equilibrium the content of flask was filtered and analyzed spectrophotometrically at 259nm.

Phase solubility study- Phase solubility studies were carried out by adding known excess amount of Furazolidone to 10 ml of solutions of β-Cyclodextrin and Hydroxy propyl β-cyclodextrin in phosphate Buffer Ph 6.8 and placed overnight in water bath incubator shaker (30rpm, 370±0.50C). The solution was filtered though micro syringe filters (#0.22micron), Then, aliquots were prepared and studied by UV-VIS spectroscopic method at 259 nm. The apparent stability constant (K_S) was calculated from the phase solubility diagrams using the following equation

$$Ks = \frac{Slope}{so(1-slope)}$$

The slope was obtained from the initial straight line portion of the plot of Furazolidone concentration against β-Cyclodextrin, and S0 is the equilibrium solubility of Furazolidone stability constant between the range of 100 and 1,000 M−1 is considered an ideal value, as smaller values indicated weak interactions between guest and CD; while a large value indicates incomplete guest release from the inclusion complex.

% Yield

Percentage yield is calculated to know about percentage yield or efficiency of any method.

$$\% \text{ Yield} = \frac{\text{Practical mass of inclusion complex}}{\text{Theoritical mass inclusion complex}} \text{ x100}$$

%Drug Content

A quantity of Inclusion Complex powder equivalent to 30 mg of Furazolidone dissolved in ph Buffer 6.8 and solution was filtered through a 0.45µm Whatman filter paper. Furazolidone content was determined by measuring the absorbance at 259 nm at UV visible spectrophotometer after appropriate dilution with pH buffer 6.8. The drug content was determined using calibration curve. The mean percent drug content was calculated as an average of three dimensions.

Evaluation Parameters for Complex Tablet

Pre Compression Parameters

Bulk Density- Weigh accurately powder and transferred in 10 ml graduated cylinder. Carefully level the inclusion complex without compacting, and read the unsettled apparent volume (V0). Calculate the apparent bulk density in gm/ml by the following formula.

$$\text{Bulk density} = \frac{Weight\ of\ powder}{bulk\ voume}$$

Batches for tablet of Furazolidone β Cyclodextrin inclusion Complex: For Selection of superdisintegrants different superdisintegrants used in different ratio and by direct compression method tablets were prepared.

Table2: Batches for tablet of Furazolidone β cyclodextrin inclusion complex

Ingredient	D1	D2	D3	D4	D5	D6	D7	D8	D9
Amount of inclusion complex Eq. To 30 mg of drug (1:2)	250	250	250	250	250	250	250	250	250
Sodium starch glycolate	1%	3%	5%	-	-	-	-	-	-
Crospovidone	-	-	-	1%	3%	5%	-	-	-
Cross Carmellose sodium	-	-	-	-	-	-	1%	3%	5%

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Microcrystalline cellulose	82	75	68	82	75	68	82	75	68
Magnesium stearate	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Talc	8	8	8	8	8	8	8	8	8
Total weight	350	350	350	350	350	350	350	350	350

Tapped Density – Weigh accurately inclusion complex and transferred in 10 ml graduated cylinder. Then tap the cylinders for 500 times primarily and measure the tapped volume (V1) to the near graduated units show again the tapping an additional 750 times and Measure the tapped volume (V2) to the nearby graduated units. If the difference between the two volumes is less than 2% then final the volume (V2) . Calculate the tapped bulk density in gm/ml by the following formula:

$$\textbf{Tapped density} = \frac{\textbf{weight of powder}}{\textbf{tapped volume}}$$

Hausner's ratio – Hausner's ratio of powder mixture was found out using the following equation

$$\textbf{Hausner's ratio} = \frac{\textbf{Tapped density}}{\textbf{Bulk density}}$$

Carr's index – it is one of the most important parameter to characteristic the nature of powders and granules. It can be calculated from the following equation

$$\textbf{Carr's index} = \frac{\textbf{Tapped density} - \textbf{Bulk density}}{\textbf{Tapped densitty}} \textbf{ x100}$$

Angle of repose – Angle of repose was found out by fixed height funnel method .The funnel height was kept constant 2 cm (h) and the diameter (d) of the circles was measured and angle of repose was find out by the equation.

$$\theta = \tan^{-1}\frac{h}{r}$$

Post Compression Parameters

Weight Variation

I.P procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determined the drug content uniformity.

Hardness

Monsanto hardness tester was used for the determination of the hardness. The tablet was placed in contact between the plungers and the handle was pressed, the Force of the fracture will record. In this work, for each formulation the hardness of 3 Tablets were evaluated.

Diameter & Thickness is measured By using Vernier caliper

Friability

A reweighed tablet was placed in the friabilator. Friabilator consists of a plastic chamber that revolves 25 rpm, dropping these tablets at a distance of 6 inches with each revolution. The tablets were rotated in friabilator for at least 4 minutes. At the end of the test tablets were dusted and reweighed, the loss in the weight of the tablet is the measure of friability and is expressed in percentage as:

$$\textbf{\% Friability} = \frac{\textbf{Loss in weight}}{\textbf{Initial weight}} \text{ x100}$$

Wetting time

A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of buffer. A tablet was put on the paper, and the time for complete wetting was measured.

Water Absorption Ratio

For measuring water absorption ratio the weight of the tablet before keeping in the petridish is noted (wb). The wetted tablet from the petridish is taken and reweighed (wa). The water absorption ratio, R can be determined according to the following equation

$$\textbf{R} = 100 \text{ x}\frac{\textbf{wa} - \textbf{wt}}{\textbf{wb}}$$

***In Vitro* Disintegration Test**

The process of breakdown of a tablet into smaller particles is called as disintegration. In vitro disintegration time was measured by dropping a tablet in a beaker containing 50 ml of phosphate

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Buffer pH 6.8 three tablets from each formulation were randomly selected and in vitro disintegration time was performed.

***In Vitro* Dissolution Study**

Randomly selected 6 tablets were subjected to drug release studies using USP dissolution apparatus, in dissolution medium volume of 900 ml was used and a temperature of 37±0.5oC was maintained. 10 ml of the sample was collected for every 5 minutes interval till 30 minutes and replaced with 10 ml of fresh buffer solution. The samples were filtered and suitably diluted and the drug assay was performed using UV spectrophotometer.

Drug Content

Weighted and crushed in a mortar then weighed powder containing equivalent of drug transferred in conical flask containing 100ml phosphate buffer pH 6.8. Its concentration 1000 mcg/ml.10ml from this stock solution was taken and diluted to 100ml Phosphate buffer pH 6.8 it makes 100µg/ml. Then Absorbance measured at 259 nm UV Spectrophotometer at 259 nm against phosphate buffer pH 6.8 blank.

Stability study of optimized Batch

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines Q1C. The stability studies were carried out on the most satisfactory formulations as per ICH guidelines Q1C. The optimized formulation wrapped in aluminum foil in and kept in humidity chamber maintained 40 ± 2 °C / 75 ± 5 % RH for 1 compatible with the drug selected for the formulation.

Result and Discussion

Spectrophotometric estimation of Furazolidone

Determination of λmax of Furazolidone:

Furazolidone was analyzed 259 nm when scanned between 200-400 nm by using UV–visible spectrophotometer as show in figure.

Calibration curve of Furazolidone

Table 3: Calibration curve

S. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	2	0.182
3	4	0.365
4	6	0.532
5	8	0.692
6	10	0.861

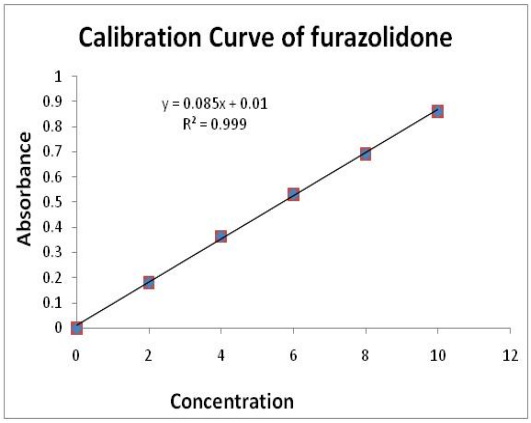

Figure 1: Calibration Curve of Furazolidone

Drug Excipient Compatibility Study

Physical Observation

The physical compatibility was observed visually. The study reveals that the drug and the excipients were physically compatible with each other as there was no change of color. The excipients are compatible with the drug selected for the formulation.

Table 4: Physical Compatibility of Furazolidone and Excipients

Drug + Excipients	Description & Condition	Room Temperature and 40°C/75% RH in days		
		Initial	15th	30th
Furazolidone	Yellow powder	NC	NC	NC
Beta Cyclodextrin	White crystalline powder	NC	NC	NC
Microcrystalline cellulose	White crystalline Powder	NC	NC	NC

Croscarmellose sodium	White powder	NC	NC	NC
Sodium starch glycolate	White powder	NC	NC	NC
Crospovidone	Creamy White powder	NC	NC	NC
Talc	White fine powder	NC	NC	NC
Mg Stearate	White fine powder	NC	NC	NC

Thin Layer Chromatography (TLC)

The Chemical compatibility was determined using TLC. The study reveals that the drug and the excipients were chemically compatible with each other as there was no significant change in the RF values. The excipients are compatible with the drug selected for the formulation.

Table 5: Thin Layer Chromatography (TLC)

S. No	Parameter	Initial	After 4 week	Observation
1	Pure Drug	Rf =0.180	Rf = 0.183	As no changes in RF value was observed hence it show no interaction after 4 week
2	Drug + Beta Cyclodextrin	Rf = 0.137	Rf = 0.138	
3	Drug + Croscarmellose sodium	Rf = 0.094	Rf = 0.097	
4	Drug + Crospovidone	Rf =0.070	Rf = 0.073	
5	Drug + Sodium Starch Glycolate	Rf =0.127	Rf = 0.129	
6	Drug + Microcrystalline Cellulose	Rf = 0.169	Rf = 0.172	
7	Drug+ Magnesium Stearate	Rf = 0.054	Rf = 0.057	
8	Drug + Talc	Rf = 0.205	Rf = 0.209	

FTIR Study

FTIR of Furazolidone

FTIR of Furazolidone + B-cyclodextrin

Drug–polymer interactions play a vital role with respect to release of drug from the formulation amongst others. FTIR techniques have been used here to study the physical and chemical interaction between drug and polymer used in Infrared (IR) spectra of Furazolidone β cyclodextrin complex. There is no significant difference in characteristic peak shown in table at wave number of drug in presence of excipients. So, it can be concluded that there was no interaction between drug and excipient in study.

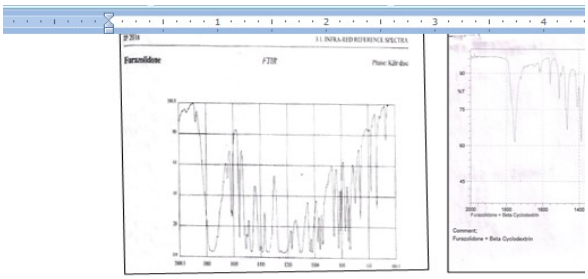

Figure 2: Reference IR spectra of Furazolidone **Figure 3: IR spectra of**

Figure 4: IR spectra of Furazolidone + β Cyclodextrins

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Precompressional parameter of complex

Evaluation of batches of Furazolidone B cyclodextrin complex

Table 6: Precompressional parameter of complex

Batch Code	Bulk Density (gm/ ml)	Tapped Density (gm / ml)	Car's index (%)	Hausner's Ratio	Angle of Repose (o)
C1	0.55	0.64	14.44	1.16	28.36±0.26
C2	0.56	0.65	14.78	1.17	29.74±0.10
C3	0.54	0.64	16.30	1.19	30.46±0.32
C4	0.53	0.63	15.17	1.18	29.39±0.24
C5	0.55	0.63	14.60	1.14	29.03±0.36
C6	0.56	0.65	12.22	1.14	28.53±0.40

Values are Expressed as Mean ± SEM; (n=3)

Since, the flow properties is important for the selection of suitable method of tablet Manufacturing. The inclusion complex tablets of Furazolidone were prepared based on Precompressional parameter of the complex of Furazolidone. Inclusion complex prepared using β cyclodextrin & HP β showed good flowability. I.e. Hausner's ratio was 1.16 to 1.20,

Angle of repose was 30.10 to 34.56°. Hence lesser amount of glidant may require in tablet manufacturing consisting of solid complexes. The Carr's index of 13.46 to 16.66 % was observed for inclusion complex indicating the good compressibility. From the values of Precompressional parameters, the direct compression technique was selected for development of inclusion complex tablet.

Solubility study

Solubility enhancement with β cyclodextrin and HP β cyclodextrin was done with different ratio (1:1, 1:2, and 1:3) and the HP β cyclodextrin (1:2) showed good result.

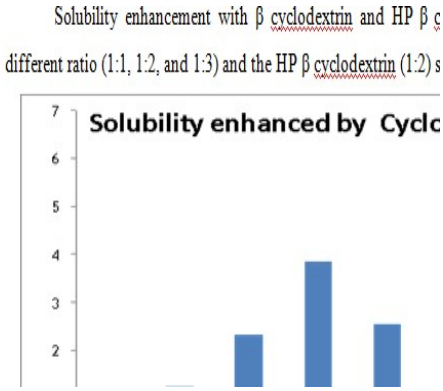

Table 7: Phase solubility study

Conc. (mmol\ml)	Solubility of Furazolidone in β Cyclodextrin (mmol/ml)	Solubility of Furazolidone in HP β cyclodextrin (mmol/ml0
0	0	0
2	0.8	2.11
4	1.25	3.32

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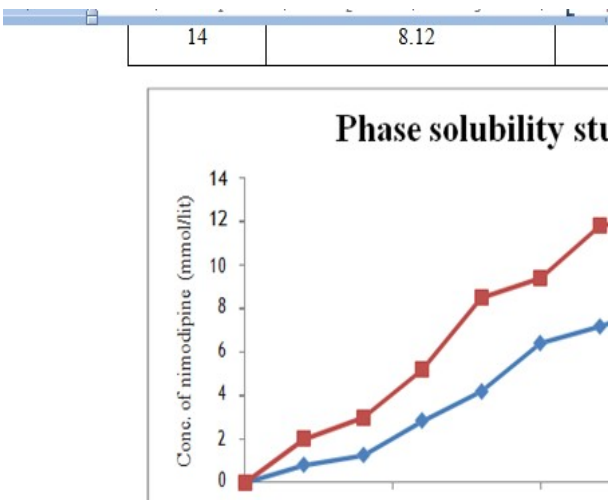
6	2.83	5.23
8	4.20	8.51
10	6.42	9.42
12	7.18	11.80
14	8.12	12.30



Stability constant of cyclodextrin

From phase solubility study we can say that the solubility of Hydroxypropyl Beta cyclodextrin was higher compare to beta cyclodextrin and the stability constant was between the ranges of 100to1000 mol-1. From the stability constant data we can conclude that the stability constant of HP BCD is higher the BCD so higher stability of complex was achieved.

Table 8: Stability constant

Name of cyclodextrin	Stability constant (Ks)
Beta cyclodextrin	312
Hydroxy Propyl beta cyclodextrin	980

Evaluation of % yield and %drug content of inclusion complex

Table 9: Evaluation of % Yield & % Drug content of inclusion complex

Batch code	% Yield	% Drug content
C1	96.23	97.21
C2	95.55	96.32
C3	93.50	97.89
C4	95.80	96.75
C5	98.56	98.70
C6	97.65	97.86

Pre-compression parameters for preliminary Batches of complex tablet

Flow property of the powder measured by the different parameter like Hausner's ratio and angle of repose. The car's index of various formulation were find as the range of 14.44 to 16.30, Hausner's ratio range is 1.14 to 1.19, and Angle of Repose range is 28.36 to30.46**.** From the result it was concluded that the powder blends had fair flow property and compressibility, addition of glidant and lubricant was done so these can be used for tablet Manufacture.

Pre-compression parameters for preliminary Batches of Furazolidone

Table 10: Pre-compression parameters

Batch code	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Avg. Weight (mg)
D1	2.3 ±0.32	0.692	2.58	348± 2.46
D2	2.3 ±0.53	0.722	2.49	346.6± 3.7
D3	2.1 ±0.31	0.685	1.92	345 ±1.16
D4	2.2 ±0.29	0.757	2.73	351.6 ±3.92
D5	2.0 ±0.54	0.832	3.02	347.23± 3.16
D6	2.4 ±0.25	0.773	2.86	350.01 ±1.28

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D7	2.3 ±0.27	0.782	2.85	352.3±1.93
D8	2.2 ±0.22	0.696	3.01	347.7±3.65
D9	2.1 ±0.32	0.688	2.91	348.2±2.47

Hardness of three tablets of each batch was checked by using Monsanto hardness tester and the data shown in table. The results showed that the hardness was found to be in the range of to 2.5 kg/cm^{2}which is in standard range. Tablets of each batch were subjected to weight variation test, difference in weight are shown in the table. The average weight of tablet was 345 to 352 mg. The results of the test showed that, the tablet weights were within pharmacopeia limit. Tablets of each batch prepared using different concentration of superdisintegrants were evaluated for percentage friability and the data is shown in the table. The test for friability of all the tablets formulation lies in the range of 0.68 to 0.83 % (less than 1 %) indicating good mechanical strength of tablets.

Disintegration time, wetting time, water absorption ratio, % drug content

Table 11: Post Compression Parameters

Batch code	In vitro disintegration time (sec)	Wetting Time(Sec)	Water absorption ratio (sec)	%Drug content
D1	50 ±1.02	22± 1.80	72 ±1.01	95.22±1.0
D2	40 ±1.28	38 ±2.12	60 ±0.37	97.62±1.0
D3	36 ±2.02	26 ±0.57	51 ±1.07	96.98±0.8
D4	34 ±1.75	31 ±1.52	55 ±0.57	96.22±1.0
D5	20±0.97	10±1.63	81 ±1.52	99.54±0.7
D6	30±1.28	29 ±2.32	62 ±2.08	98.00±1.0
D7	28±1.37	15±2.5	80.55±0.3	97.35±0.8
D8	30±1.25	22±1.70	75.22±1.4	98.80±1.0
D9	52±1.45	41±1.65	78.55±0.8	97.62±1.0

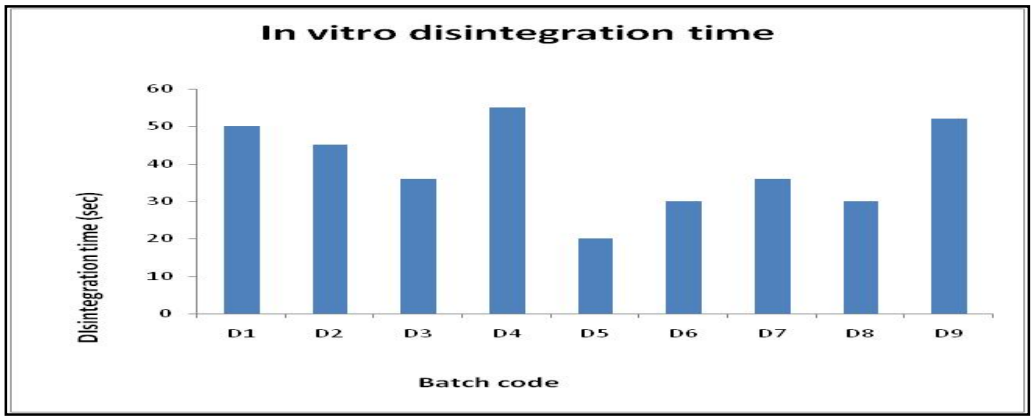

Figure 7: In vitro disintegration time

The most important parameter that is needed to optimize during the development of inclusion complex tablets is disintegration time which desired to be less than 60 seconds, Here disintegration of tablets occur within 20 to 52 seconds and the order disintegration time Crospovidone < Cross Carmellose sodium < SSG. As the concentration of superdisintegrants in the formulations increased the disintegration time was found to decrease. Wetting time is used as an indicator from the ease of the tablet disintegration in buccal cavity. It was observed that wetting time of tablets was in the range of 10 to 41 seconds. Drug content of all prepared tablets was found to be in the range of 92.98 to 99.30 %with high content uniformity. From the above data

crospovidone showed best performance on inclusion complex tablet. D5 batch having 5% crospovidone and have less disintegration time there for it was optimized batch.

In vitro dissolution profile of Furazolidone inclusion complex

Table 12: In vitro dissolution profile of Furazolidone containing inclusion complex

Batch Code	% Cumulative drug release						
	Time (min)						
	00	5	10	15	20	25	30
D1	00	43.63	58.38	66.58	74.52	78.54	95.31
D2	00	41.25	53.15	63.73	75.70	83.22	93.32
D3	00	55.65	63.31	71.50	80.64	86.65	96.55
D4	00	53.11	67.42	80.48	86.65	91.50	97.18
D5	00	62.37	75.43	88.58	93.29	97.92	99.21
D6	00	58.52	66.56	74.68	85.66	94.73	98.62
D7	00	43.54	56.11	68.21	77.55	82.47	95.59
D8	00	54.89	70.23	83.65	90.69	95.21	95.25
D9	00	41.25	52.15	64.78	75.70	83.22	93.32

Stability study for optimized formulation:

The direct compressed fast dissolving tablet of Furazolidone containing crospovidone 5% Batch D5 was optimized batch and as per formula of optimized batch were subjected to stability studies.

Table 13: Stability study of final formulation (D5)

Parameters	**0 days**	**After 90 days at 40 ± 2°C and 75 ±5° RH**
Hardness (kg/cm2)	2.20	2.19
In vitro disintegration time (sec)	20±0.97	21±0.95
Wetting time (sec)	10±1	12±1
In vitro dissolution	**% cumulative drug release**	
Time (min)	0 days	**After 30 days**
0	0	0
5	62.37	59.32
10	75.43	72.12
15	88.58	85.9
20	93.29	94.13
25	97.92	98.20
30	99.21	98.98

The prepared complex tablet of Furazolidone was packed in aluminum strip and subjected for short term stability studies at 40 ± 2°C and 75 ±5° RH for 1 month in humidity chamber. Sample withdrawn after 30 month showed no significant change in appearance of tablets drug release CPR profile of stability studies are shown disintegration time was 15 sec, wetting time was 10 sec and optimized batch drug release profile was 99.54. The results of short term stability studies indicated that the formulation was stable on required storage condition.

Conclusion

Identification of functional group of the drug can be done by FTIR Spectroscopy. Formulation of complex of poorly soluble drug Furazolidone prepared by the inclusion complex with different molar ratio (1:1) (1:2) (1:3) β Cyclodextrin and HP β cyclodextrin using kneading method.

The prepared complex was evaluated % Yield, %Drug Content, solubility study, Phase solubility study. Furazolidone complex prepared with HP β Cyclodextrin (1:2) was found to be best complex then other complex.

The optimized complex was further evaluated for their physiochemical characterization such as a physical observation, TLC, FTIR spectroscopy. For Preparation of Furazolidone tablet and it was found that direct compression method was suitable for Furazolidone tablet because of good flow properties.

Formulation of Furazolidone tablet is done by using super Disintegrant such as crospovidone, sodium starch glycolate, croscarmellose sodium in different concentration. The prepared formulation were evaluated for hardness, thickness, weight variation, friability, in-vitro disintegration time , drug content, in-vitro drug release and on the basis of that Formulation D5 containing crospovidone 5% concentration was found to be best then other formulation.

The optimized formulation was evaluated for their stability studies. The optimized formulation was stable at room temperature & environmental condition.

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