International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 6(4): July-August 2016

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Research Article……!!!**

Received: 20-07-2016; Revised: 29-08-2016; Accepted: 30-08-2016

FORMULATION AND EVALUATION CAPSULES CONTAINING CUBOSOMES OF OMEPRAZOLE FOR IMPROVING IT'S BIOAVAILABILITY

Amala Tom*, Sujith Abraham

Nirmala College of Pharmacy, Muvattupuzha.

Keywords:

Omeprazole; Cubosomes; Poloxamer 407; Glyceryl monooleate; bioavailability

For Correspondence:

Amala Tom

Nirmala College of Pharmacy, Muvattupuzha

E-mail:

amalatom392@gmail.com

ABSTRACT

Proton pump inhibitors (PPIs) are one of the most commonly prescribed classes of medications in the primary care setting and are considered a major advance in the treatment of acid-peptic diseases.Omeprazole is a unique and effective agent for suppression of gastric acid secretion. It promises to be especially useful in Zollinger-Ellison Syndrome and in other patients who have failed to respond to H_2 antagonist therapy. The dose requirement for Zollinger-Ellison syndrome (ZES) disease is upto 120 mg per day. The drug omeprazole shows biological half life of 0.5- 1 hours. Considering it's proven therapeutic efficacy for ZES disease, this study attempted to formulate controlled release capsule containing cubosomal granules with improved bioavailability. Omeprazole comes under BCS classification II, that is it has a low water solubility and high permeability. This low water solubility is the reason for it's low bioavailabiity. So formulating omeprazole into cubosomes will enhance it's water solubility and thereby improve it's bioavailability. Cubosomes are discrete submicron nanostructured particles formed from cube forming lipids like monoolein with water. Isotropic dilution method is followed to prepare cubosomal dispersion and the dispersions were optimized based on evaluation parameters like drug content, *in vitro* drug release, entrapment efficiency, and SEM analysis. Then the optimized dispersion was converted to granules using starch and are filled into hard gelatin capsule shells.Capsules are finally enteric coated with organic solution of Eudragit L 100. Evaluation of enteric coated capsules were carried out.

INTRODUCTION

In this work an attempt was made to formulate and evaluate cubosomes containing an antiulcerative drug, Omeprazole for improving its bioavailability and to provide controlled drug release over 24 hours. The main objective of the study was to enhance oral bioavailability and solubility of the drug. Omeprazole comes under BCS classification II, that is low solubility and high permeability. Preparing cubosomes of Omeprazole will improve the solubility and thereby the bioavailability.

MATERIALS AN METHODS

The drug Omeprazole and the excipients poloxamer 407, Glyceryl monooleate were bought from Chemdyes corporation, Rajkot.

Determination of standard calibration curve of Omeprazole [1]

About 10 mg of pure drug omeprazole was weighed and transferred in to a 10ml volumetric flask. The drug was dissolved completely in a few ml of Methanol and made up to the final volume with Methanol to get a stock solution of concentration 1000µg/ml.

From the stock solution 0.5, 1, 1.5, 2,and 2.5ml aliquots of standard stock solution were pipetted out to 100ml volumetric flask and made upto the volume with water to get the final concentrations 5, 10, 15, 20 and 25µg/ml respectively. Absorbance was recorded (UV spectrometer) by using water as reference. The standard plot was obtained by plotting concentration in µg/ml vs absorbance at scanned λmax 296 nm.

PRE-FORMULATION STUDY

Preformulation studies were performed for the obtained sample of drug for identification and compatibility studies.

Identification of Pure Drug

a. Determination of melting point:

Melting point of Omeprazole was determined by capillary method.

b. Identification by FTIR spectroscopy[2]

FTIR spectral analysis of pure drug was carried out. The peaks obtained in the spectrum were compared with the standard spectrum of omeprazole.

Physicochemical parameters

a. Organoleptic properties

The physical appearance of drug was observed and compared with the pharmacopoeial specifications.

b. Solubility of Omeprazole[3]:

Preformulation solubility analysis was done to select a suitable solvent system to dissolve the drug and also to test its solubility in the dissolution medium which was to be used. Solubility of Omeprazole was determined in various solvents like dichloromethane, chloroform, ethanol, methanol, water.

Compatibility Studies

Fourier Transform Infrared Spectroscopic (FTIR) analysis

The FTIR spectrums of Omeprazole was studied by using Fourier Transform Infrared (FTIR) spectrophotometer (Perkin Elmer, spectrum-100, Japan) using the KBr disk method (5.2510 mg sample in 300.2502 mg KBr). The FTIR spectra was recorded over the wavelength range of 400-4000 cm-1 using FTIR spectrometer. FTIR spectral analysis of pure drug and polymers was carried out individually and also in combination, observation was made whether changes in the chemical constitution of drug after combining it with the polymers occurred. The peaks in spectrum were compared with the standard spectrum of pure drug.

Preparation of Omeprazole cubosomes[4]

The prototype formulations were prepared by varying glyceryl monooleate and poloxamer. The formula of composition is mentioned in table. In the first trial the Glyceryl monooleate was used at 10% and increased by 5% for each subsequent trial up to 40%. In the 7th formulation 15% GMO is used and poloxamer 407 concentration is increased from 2 to 5%. The process used for preparation of cubosome dispersion is isotropic dilution method : here the oil phase inclue GMO, ethanol, and water and the aqueous phase include poloxamer 407 an water. Mixing Instruction is as follows: Weigh the oil phase ingredients into a suitable vessel equipped with a mixer. The materials form a clear, low viscosity isotropic liquid. Combine the aqueous phase ingredients into a separate vessel and stir until all polymer is dissolved. Introduce aqueous phase solution into oil phase and homogenize at 3000 rpm for 10 minutes to produce cubosomes of the desired size. A colloidally stable dispersion of cubosomes forms.

Formulation of cubosome dispersions

Formulation code	Glyceryl monooleate %w/w	Poloxamer 407 w/w	Ethanol ml	Omeprazole g	Water upto 100%
F_1	10	1	5	5	100
F_2	15	1	5	5	100
F_3	20	1	5	5	100
F_4	30	1	5	5	100
F_5	40	1	5	5	100
F_6	50	1	5	5	100
F_7	15	2	5	5	100
F_8	15	3	5	5	100
F_9	15	4	5	5	100
F_{10}	15	5	5	5	100

Evaluation of cubosomal dispersions

1. **Drug content**[5]

   Omeprazole loaded cubosomes were mixed with methanol and sonicated for 10 min to obtain a clear solution. Concentrations of Omeprazole were determined spectrophotometrically at λ_{max} 296 nm.

2. **Entrapment Efficiency (EE)**[6]

   Entrapment efficiency is defined as the percentage amount of drug which is entrapped by the cubosomes. For the determination of entrapment efficiency, the un-entrapped drug was first separated by centrifugation at 15000 rpm for 30 minutes. The resulting solution was then separated and supernatant liquid was collected. The collected supernatant was then diluted appropriately and estimated using UV visible spectrophotometer at 296 nm.

   The percent of encapsulation efficiency (EE %) was determined by the following equation:

$$\%\mathrm{EE} = \frac{\{[\text{total drug}] - [\text{free drug}]\}}{\text{total drug}} * 100$$

3. ***In vitro* drug release** [7]

   Studies were performed for all the formulations. *In vitro* release studies were carried out using bichambered donor receiver compartment model (Franz diffusion cell) and this was placed on magnetic stirrer and temperature was adjusted to 37 ± 0.50 C. One end of the chamber was covered with Himedia dialysis membrane (cut-off molecular weight:

12000-14000), which was previously soaked in phosphate buffer pH 6.8. Phosphate buffer pH 6.8 was placed in the receptor cell. Accurately measured 5ml of the formulation placed on a dialysis membrane, which was in contact with receptor medium. Samples were withdrawn at specified time intervals and the medium was compensated with phosphate buffer pH 6.8. The samples were analyzed for drug using a UV-Vis spectrophotometer at 296 nm.

4. **Vesicle shape and size analysis of cubosomes[8]:**

Size and shape of the cubosomes were determined using optical microscopy and SEM (JEOL JSM6390). For studying the morphology and surface topography, the prepared cubosomes were coated with gold – palladium under an argon atmosphere at room temperature and the SEM of cubosomes were taken to illustrate its ultra structure.

Optimization of prepared cubosomes

The prepared cubosomal dispersions were optimized based on the evaluation parameters.

Peparation of Omeprazole loaded cubosomal oral capsules[9,10]

Optimized cubosomal formulation (15% GMO and 1% poloxamer 407) was selected for preparation of granules. To the optimized cubosomal formulation, starch was added to obtain a wet mass. Then the wet mass was passed through sieve no.16 to form granules. The granules were air dried at room temperature and were filled into '0' sized capsules.

Evaluation of Omeprazole loaded oral capsules

1. **Derived properties and Flow properties**

Derived properties

Bulk Density and Tapped density

Both loose bulk density (D_b) and tapped bulk density (Dt) was determined. A quantity of 51 gm of granules, previously shaken to break any agglomerates formed, was introduced in to 100 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2 cm at 2 second intervals. Tapping was continued until no further change in volume was noted. Db and Dt were calculated using as the following equations.

Db = Weight of the powder blend /Untapped Volume of the packing

Dt =Weight of the powder blend /Tapped Volume of the packing

Flow properties

Compressibility Index

It is a simple test to evaluate the D**t and D_b** and the rate at which it packed down. The formula for Carr's Index is as below

$$\mathbf{I=\frac{(Dt-Db)}{Dt} * 100}$$

Where, Dt is the tapped density of the powder,

Db is the bulk density of powder

Hausner's Ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula**.**

Hausner ratio = Dt / Db

Effect of Carr's Index and Hausner's Ratio on flow property

Carr's Index (%)	Flow Character	Hausner's Ratio
< 10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
126–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very, very poor	>1.60

Angle of Repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blends were allowed to flow through the funnel freely on to the surface. The diameter of the powder blend cone was measured and angle of repose was calculated using the following equation.

$$\mathbf{\tan \theta = h / r, \quad \theta = \tan^{-1}(h / r)}$$

Where, h = height of the powder cone.

r = radius of the powder cone.

Relationship between angle of repose and flowproperties[11]

Angle of repose	Powder flow
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very poor

2. Drug Content

Granules (equivalent to 100mg of the drug) were accurately weighed and transferred into a 100ml volumetric flask and 10ml of methanol was added to dissolve the drug. The solution was made up to volume with pH 6.8 phosphate buffer. The resultant solution was filtered and suitably diluted and analyzed using UV Visible spectrophotometer at 296nm using pH 6.8 phosphate buffer as a blank.

3. *In vitro* Dissolution Studies [13]

Apparatus : USP dissolution test apparatus type-II

Medium :900ml

Speed and time :100 rpm and 24 hrs

Prepared enteric cubosomal oral capsules coated capsules were evaluated for their integrity in the physiological environment of stomach and small intestine. This study was carried out using USP dissolution test apparatus type-II .The capsules were tested for drug release in 0.1N HCl (900 ml) for first 2 hrs as average gastric emptying time is 2 h, then dissolution media was replaced with 6.8 pH phosphate buffer (900 ml) for 24 hrs. At the end of respective time periods, each sample of 5 ml were taken at specified 1 hr intervals and analysed for Omeprazole content at 296 nm using UV spectrophometer..

4. Kinetic Modelling [14,15,16]

Toanalyzethedrugreleaseratekineticsandmechanismofdrugreleasefrom the cubosomal oral capsules,the*invitro*drug releasestudiesdatawasfittedintoZeroorder,First order,Higuchi model, Hixson-Crowell CubeRootLaw model,andKorsmeyerpeppasmodels.From these,best-

fitmodelswereselected.

The quantitative interpretation of the values obtained in the dissolution assay is facilitated by the usage of a generic equation that mathematically translates the dissolution curve in the function of some other parameters related with the pharmaceutical dosage forms. The kind of drug, its polymorphic form, crystallinity, particle size, solubility and amount in the pharmaceutical dosage form can influence the release kinetics.

Interpretation of Diffusional release mechanisms from Formulations.

Release exponent (n)	**Drug transport mechanism**
0.5	Fickian diffusion
0.5 < n <0.89	Non -Fickian transport
0.89	Case II transport
Higher than 0.89	Super case II transport

5. Accelerated Stability Studies

Accelerated stability studies for optimized cubosomal oral capsules containing 100mg Omeprazole were conducted as per ICH guidelines at 40°C ±2°C / 75%±5% RH at sampling intervals of 30, 60 and 90 days respectively. The drug content and *in vitro* release was determined periodically.

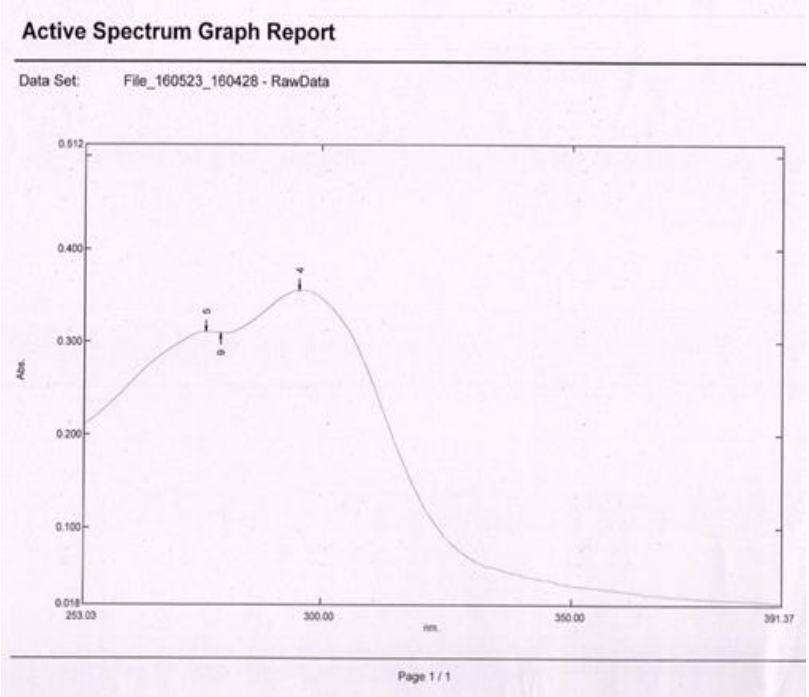
RESULTS AND DISCUSSION

A successful attempt was made to formulate ten formulations of cubosomes using different concentration of Glyceryl monooleate and poloxamer 407 composition.

The formulations are subjected to evalution parameters which are discussed below.

Development of standard calibration curve of Omeprazole at 296 nm.

The absorption maximum of the standard solution was scanned between 200-400nm regions on UV- Visible spectrophotometer. The wavelength of maximum absorbance (λ_{max}) was found to be 296 nm.



λ_{max} of Omeprazole

The calibration curve of drug was obtained. First, Beer-Lambert's range was determined by preparing series of solutions of various concentrations and it was found that law was obeyed within the concentration range of 5-25 µg/ml. The data obtained was statically evaluated to calculate the correlation coefficient (R^2) and it was found to be 0.9991.

Data for calibration curve of Omeprazole at 296 nm

Sl. No	Concentration µg/ml	Absorbance
1	5	0.172
2	10	0.369
3	15	0.580
4	20	0.784
5	25	0.990

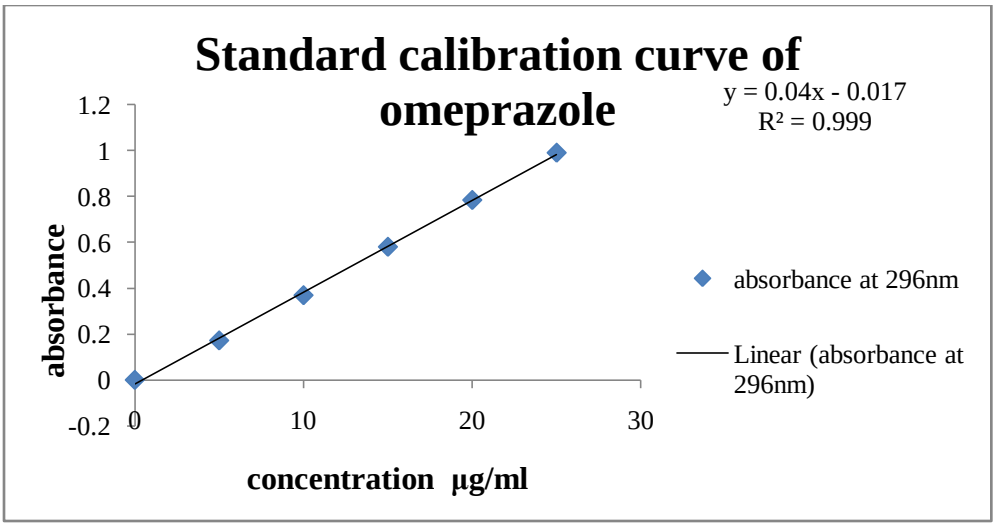


Figure 28 : Standard graph of Omeprazole

Pre- formulation study

Identification of pure drug

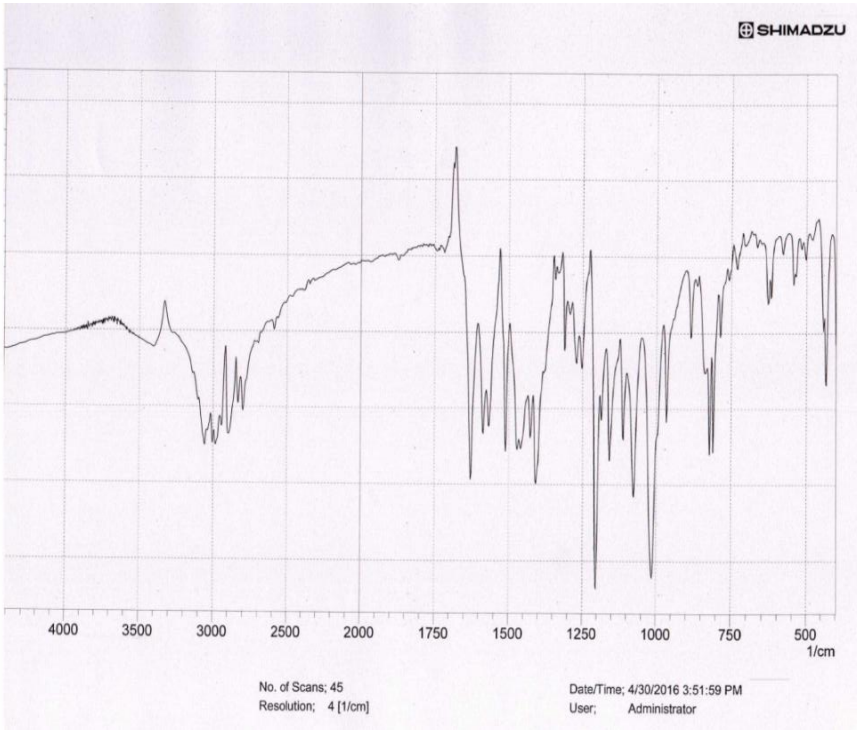
1. **Melting point**

The melting point of Omeprazole was determined by capillary method (in triplicate) and found to be in the range of 156- 157° C (with decomposition). Thus obtained melting point is in agreement with literature melting point which indicates the purity of drug.

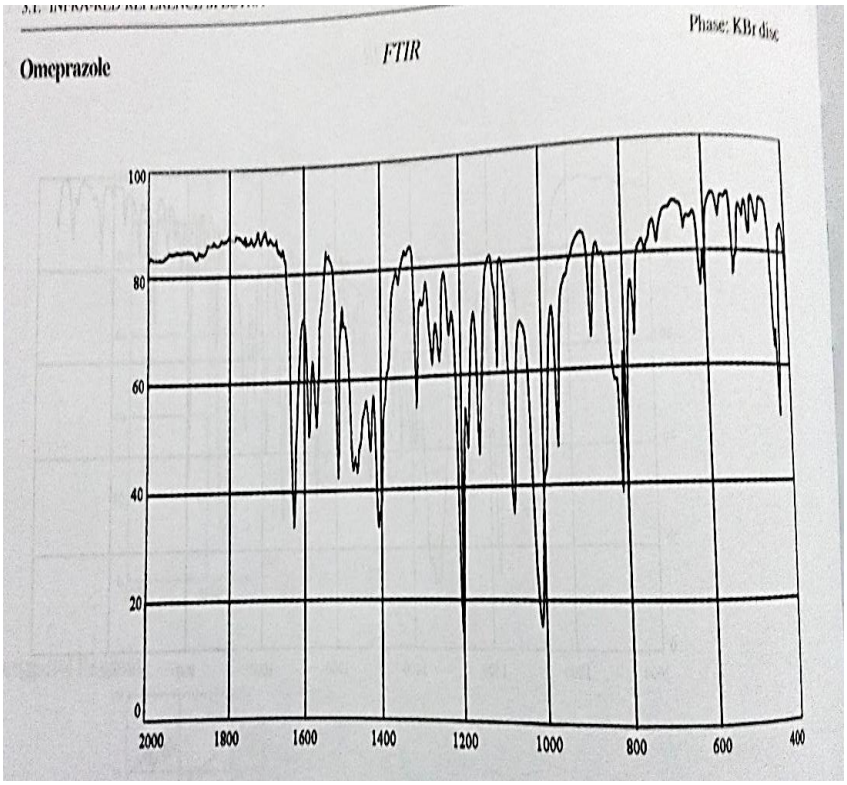
2. **Identification by FTIR spectroscopy**

From the FTIR spectra of the pure drug and the standard spectrum of the drug, it was observed that all the characteristic peaks of Omeprazole standard spectrum was present in the spectrum of Omeprazole indicating that the obtained drug is pure.

FTIR Spectra of Omeprazole



Standard FTIR spectrum of Omeprazole[17]



Physicochemical Parameters:

a. Organoleptic Properties:

Omeprazole was found to be white, almost white crystalline powder. The physical appearance complied with the reference specifications.

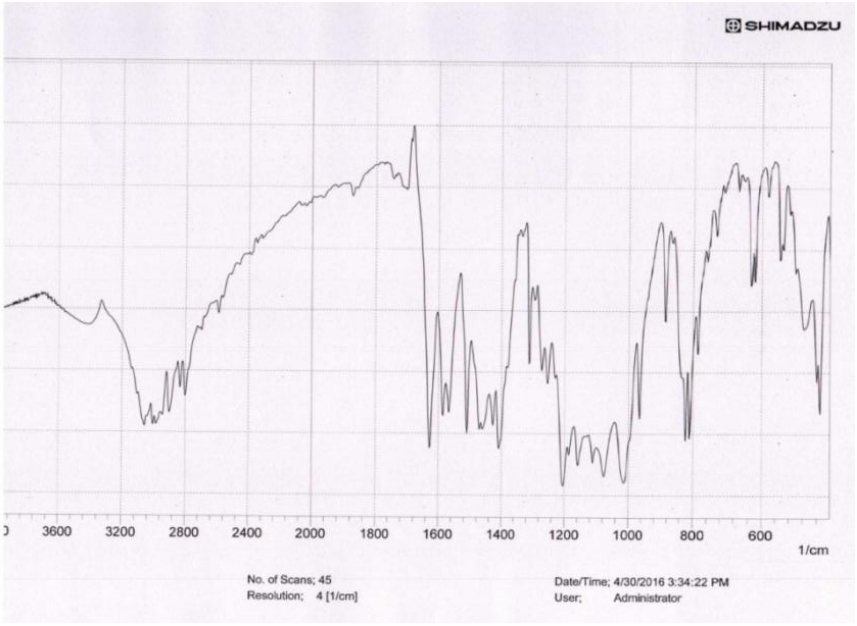
b. Determination of solubility

Freely soluble in dichloromethane & in chloroform; soluble in ethanol (95%) and in methanol; very slightly soluble in water. It dissolves in dilute solutions of alkali hydroxides.

Determination of Drug Excipient Compatibility by FTIR Spectroscopy

The individual FTIR spectra of the pure drug Omeprazole, as well as the combination spectra of the drug and excipient are shown in the figures.

FTIR Spectra of Omeprazole loaded cubosomal Capsules



From the FTIR spectra of the pure drug and the combination spectra of the drug with the excipients, it was observed that all the characteristic peaks of Omeprazole were present in the combination spectra indicating the compatibility of the drug with the excipients used.

Preparation of cubosome Formulations

Cubosome formulations using different ratio of poloxamer 407, glyceryl monooleate were prepared by isotropic dilution method followed by homogenization at 3000 rpm. A white opaque homogeneous formulations without any visible particulates were generated. The formulations were optimized on the basis of drug content entrapment efficiency and *in vitro* drug release.

Optimized cubosome dispersion (F_6)

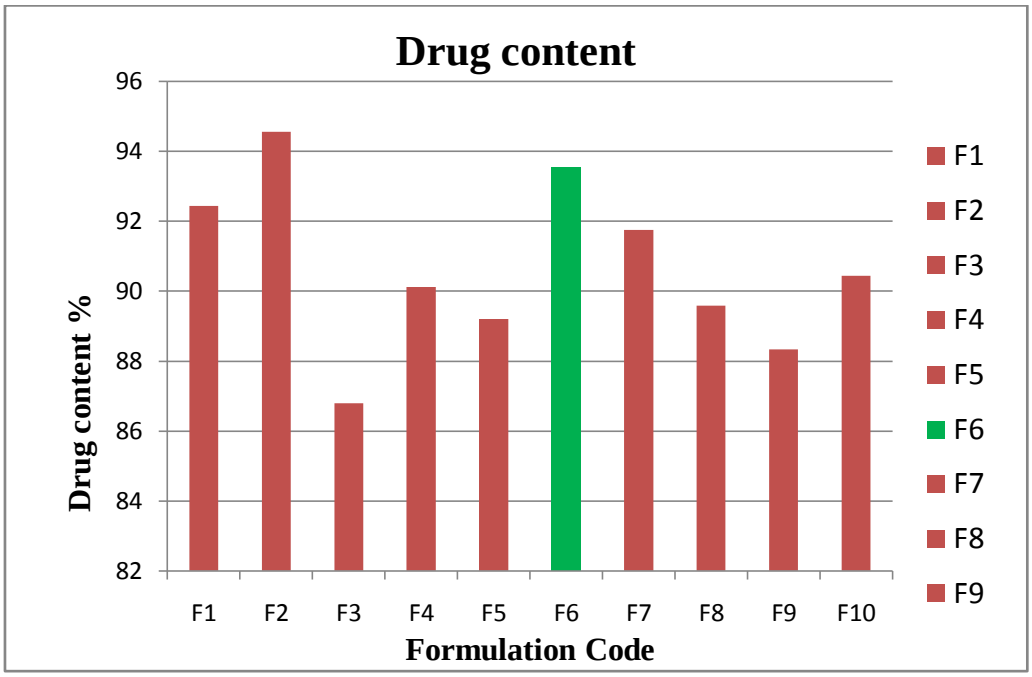
EVALUATION OF CUBOSOMES

1. Drug Content

Irrespective of difference in composition, the drug content of formulations F_1 to F_{10} was found in range 86.79 to 94.56 %. Formulation F_6 showed highest % drug content and is 93.55 %.

Formulation code	Drug content
F_1	92.45
F_2	94.56
F_3	86.79
F_4	90.12
F_5	89.2
F_6	93.55
F_7	91.76
F_8	89.59
F_9	88.34
F_{10}	90.45

Drug content of prepared cubosome dispersions



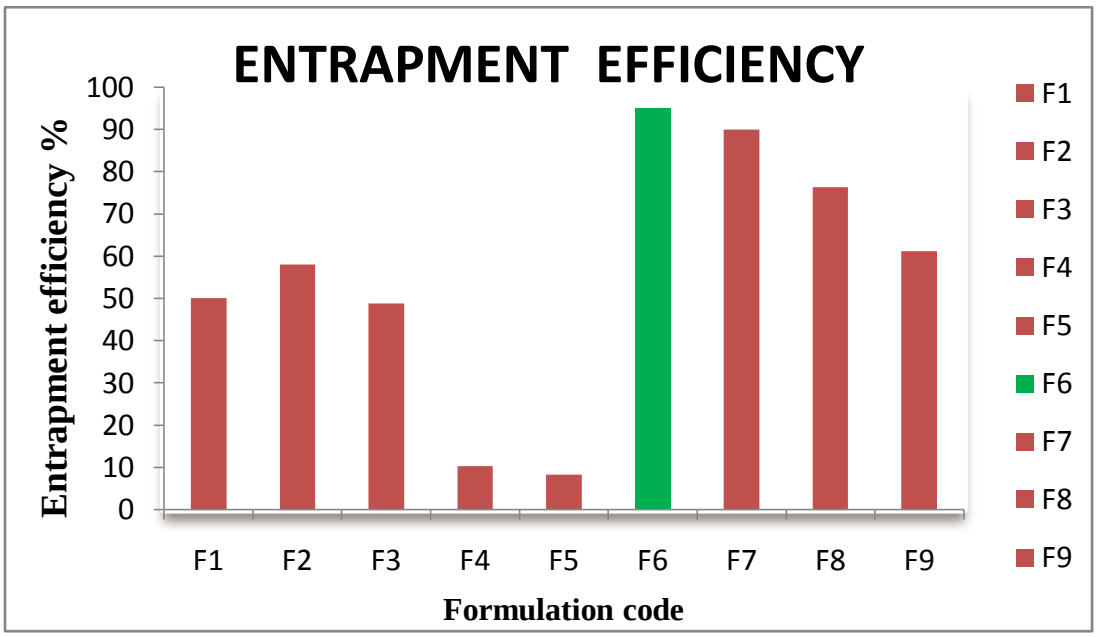
Drug content of prepared cubosome dispersions

2. Entrapment efficiency

Entrapment efficiency ranges from 8.3-94.9. Maximum entrapment efficiency was found for F_6. As GMO concentration increases entrapment efficiency decreases.Similarly as Poloxamer 407 increases entrapment efficiency decreases.

FORMULATION CODE	ENTRAPMENT EFFICIENCY %
F_1	50.02
F_2	58
F_3	48.856
F_4	10.288
F_5	8.3
F_6	94.9
F_7	89.86
F_8	76.35
F_9	61.19
F_{10}	52.37

Entrapment Efficiency of Cubosome dispersions



Entrapment Efficiency of Cubosome dispersions

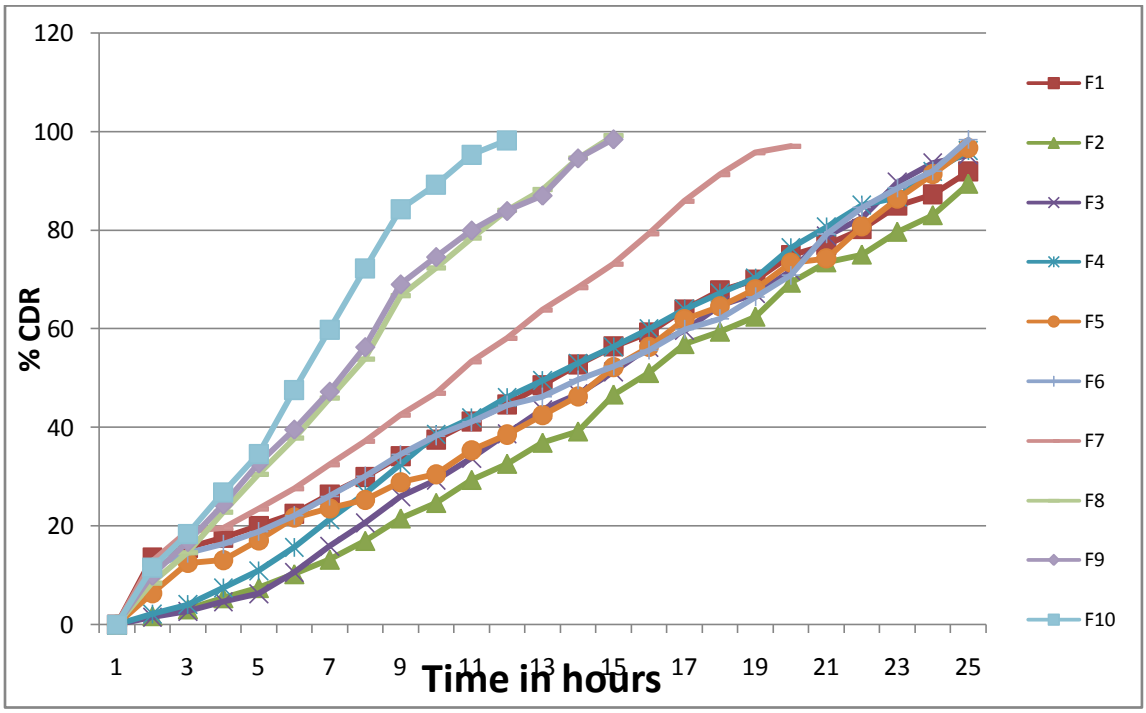
3. *in vitro* release study

Formulation F_7, F_9, F_{10} show fast drug release.Formulation F_1, F_2, F_3, F_4, F_5, F_6 shows controlled release.

Time in hours	Cumulative % drug release									
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}
0	0	0	0	0	0	0	0	0	0	0
1	13.62	1.75	1.5	2.13	6.43	11.75	12.87	8.44	9.93	11.62
2	15.56	3.12	2.75	4.06	12.5	14.5	18.93	14.59	16.78	18.37
3	17.68	5.38	4.63	7.44	13.13	16.31	19.56	22.86	24.38	26.83
4	20.06	7.44	6.31	10.89	17.06	18.88	23.5	30.54	32.71	34.61
5	22.5	10.25	10.63	15.69	21.69	22.13	27.56	37.82	39.58	47.63
6	26.44	13.19	15.94	21.31	23.62	26.06	32.43	45.93	47.27	59.8
7	29.94	17	20.69	26.69	25.34	30.13	37.19	53.9	56.31	72.28
8	34.13	21.56	26.00	32.50	28.92	34.56	42.5	66.7	69.04	84.26
9	37.54	24.70	29.35	38.60	30.54	38.29	46.92	72.38	74.59	89.3
10	41.23	29.37	33.75	41.94	35.37	41.13	53.39	78.46	79.97	95.37
11	44.63	32.64	38.75	46.09	38.56	44.54	58.12	84.02	83.92	98.26
12	48.59	36.91	43.60	49.49	42.48	46.21	63.89	88.27	87.05	
13	52.74	39.20	46.8	53.04	46.31	49.69	68.39	94.70	94.60	
14	56.42	46.69	51.30	56.38	52.21	52.42	73.16	99.20	98.47	
15	59.24	51.05	56.30	59.98	56.36	55.67	79.31			
16	63.94	56.92	59.7	64.05	61.96	59.92	85.90			
17	67.81	59.43	64.80	67.30	64.56	62.07	91.37			
18	69.96	62.48	67.20	70.34	68.06	66.52	95.8			
19	74.90	69.36	71.80	76.50	73.40	70.89	97.06			

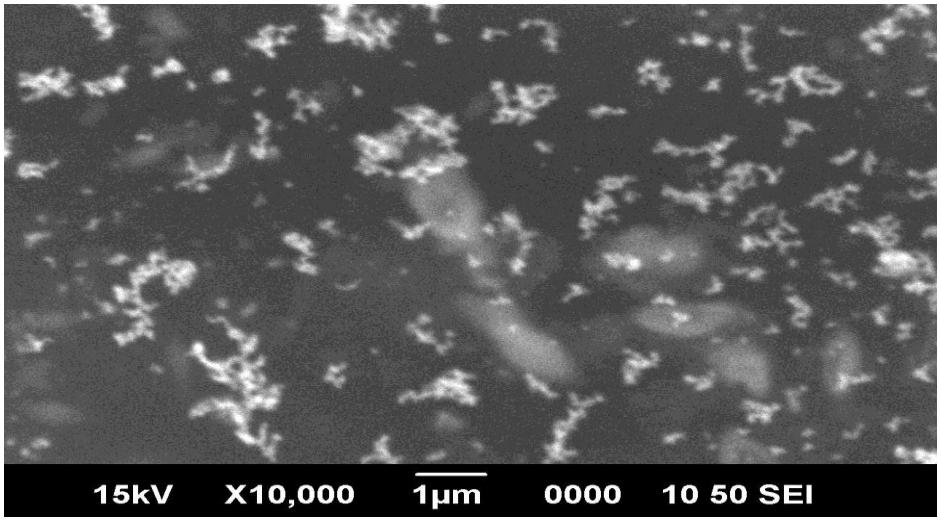
20	77.05	73.50	78.90	80.65	74.27	79.30				
21	80.26	75.07	82.51	85.15	80.79	84.62				
22	84.97	79.69	89.79	86.74	86.42	88.63				
23	87.30	83.06	93.68	91.99	91.37	92.05				
24	91.93	89.43	95.31	96.16	96.70	98.45				

***In vitro* drug release study of cubosome dispersions**



***In vitro* drug release study of cubosome dispersions**

4. Morphological analysis - SEM analysis



SEM images of cubosome dispersion F_6

The 10000x magnification image obtained from SEM Analysis shows nano sized cubosomes. Therefore the method selected is apt for preparation Omeprazole loaded cubosomes.

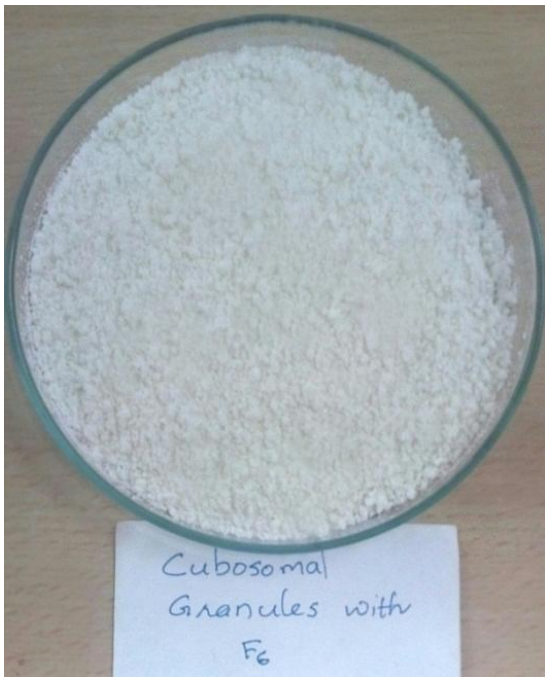
Optimization of cubosomal dispersion

Formulation F_6 is optimized based on entrapment efficiency, drug content and *in vitro* release study.

Formulation F_6 shows

Entrapment efficiency	:	94.5%
Drug content	:	93.55%
In vitro drug release at 24th hour	:	98.45%

Preparation and Characterization of granules



Cubosomal granules with F_6

Derived properties and flow properties

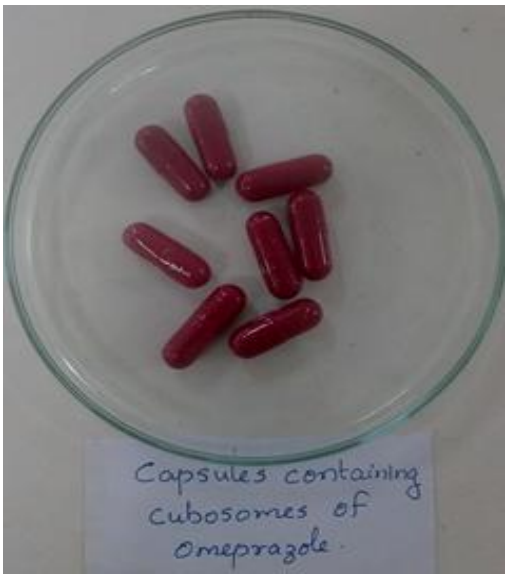
Sl.No	Properties	Granules with F_6
1	Angle of repose	24.94˚
2	Bulk density	1.14
3	Tapped density	1.27
4	Hausner's ratio	1.11
5	Carr's index	10.23

Flow properties of cubosomal granules

Drug content

Drug content of prepare granules were found to be 92.64%.

Preparation and Evaluations of capsules



Capsules containing cubosomes of Omeprazole

1. **Uniformity of weight**

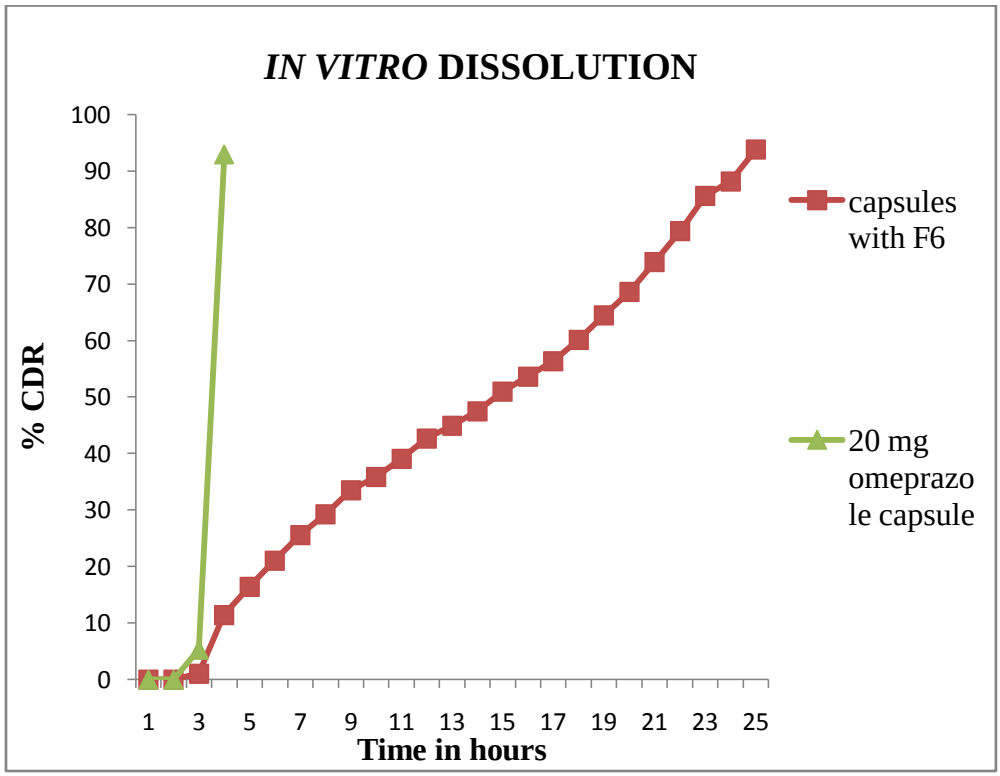
Average weight of capsules was found to be 898.56 mg.No capsule deviate from the average weight by ±7.5%. Therefore the capsules comply with the test for uniformity of weight in Indian pharmacopoeia.

2. ***In vitro* dissolution study**

Time in hours	Cumulative % drug release	
	Capsules with F_6	20mg omeprazole capsules
0	0	0
1	0	0
2	0	5.3
Buffer medium(Phosphate buffer 6.8 pH)		
3	11.43	93.0
4	16.40	
5	21.04	
6	25.59	
7	29.31	
8	33.56	
9	35.84	
10	39.07	
11	42.64	
12	44.93	

13	47.46	
14	50.97	
15	53.63	
16	56.39	
17	60.19	
18	64.48	
19	68.67	
20	73.95	
21	79.42	
22	85.67	
23	88.19	
24	94.86	

***In vitro* Dissolution study of cubosomal capsules and plain capsules**

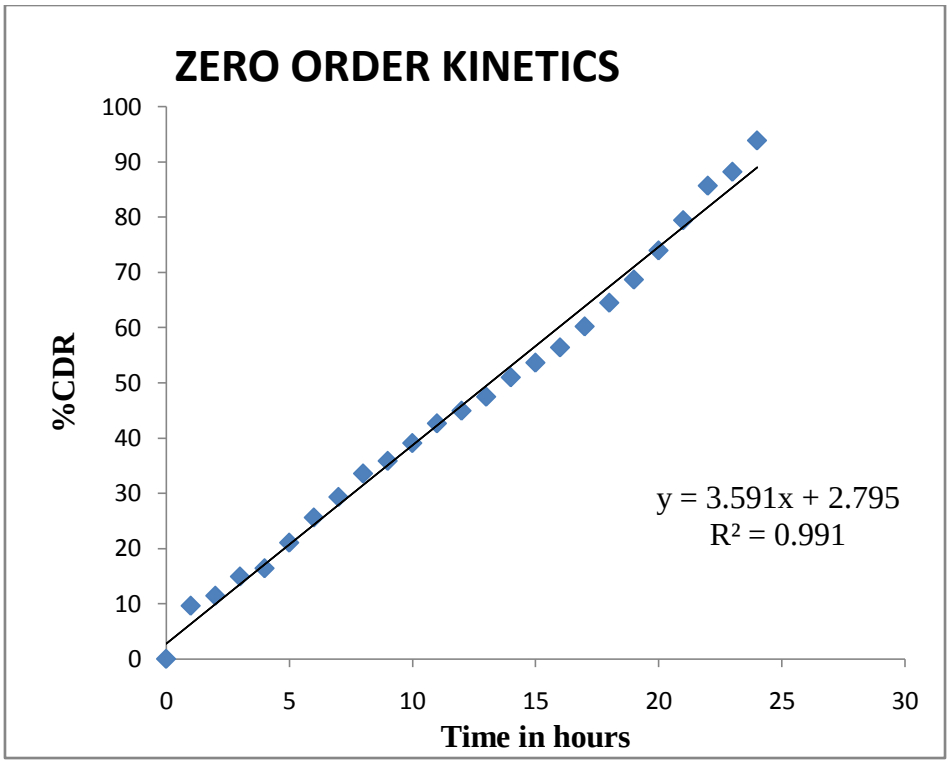


***In vitro* Dissolution study of cubosomal capsules and plain capsules**

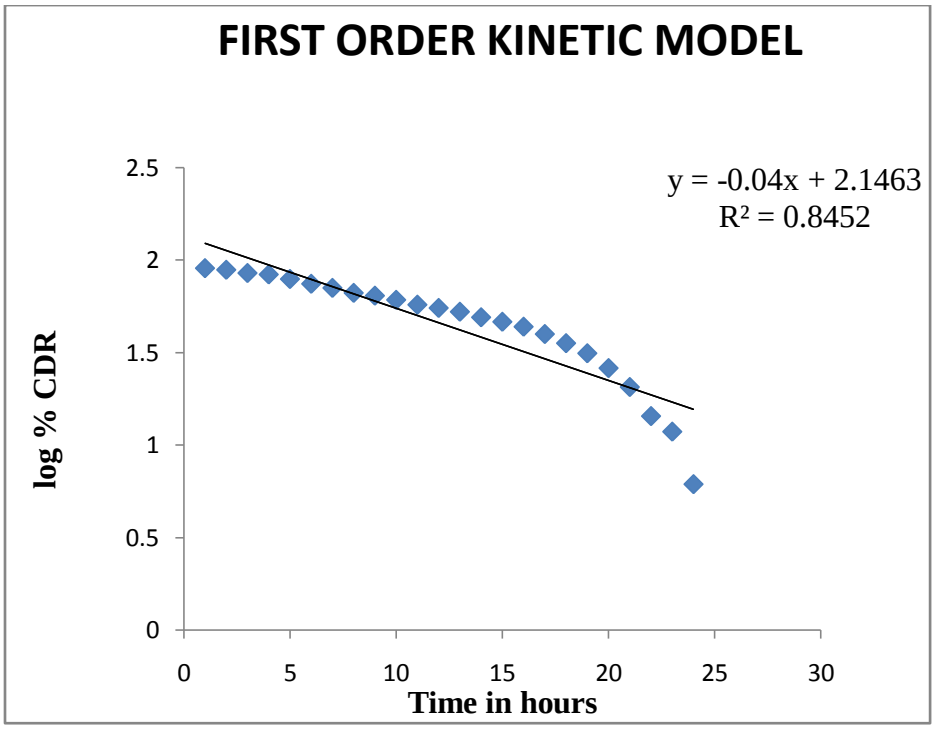
3. Kinetic study

The results obtained from *in-vitro* dissolution studies were plotted in different kinetic models.

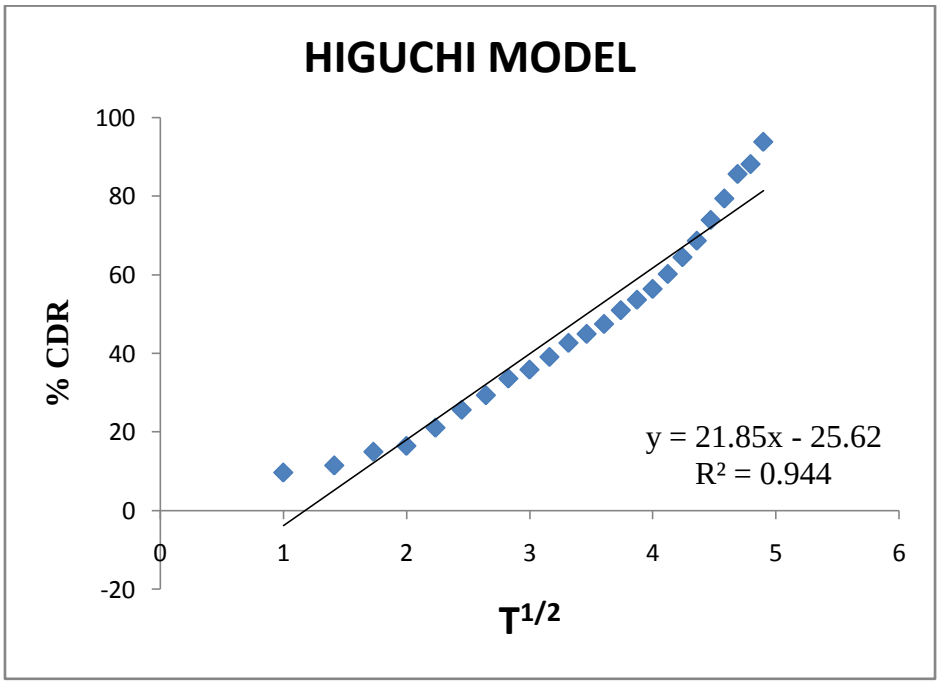
Zero order kinetic model



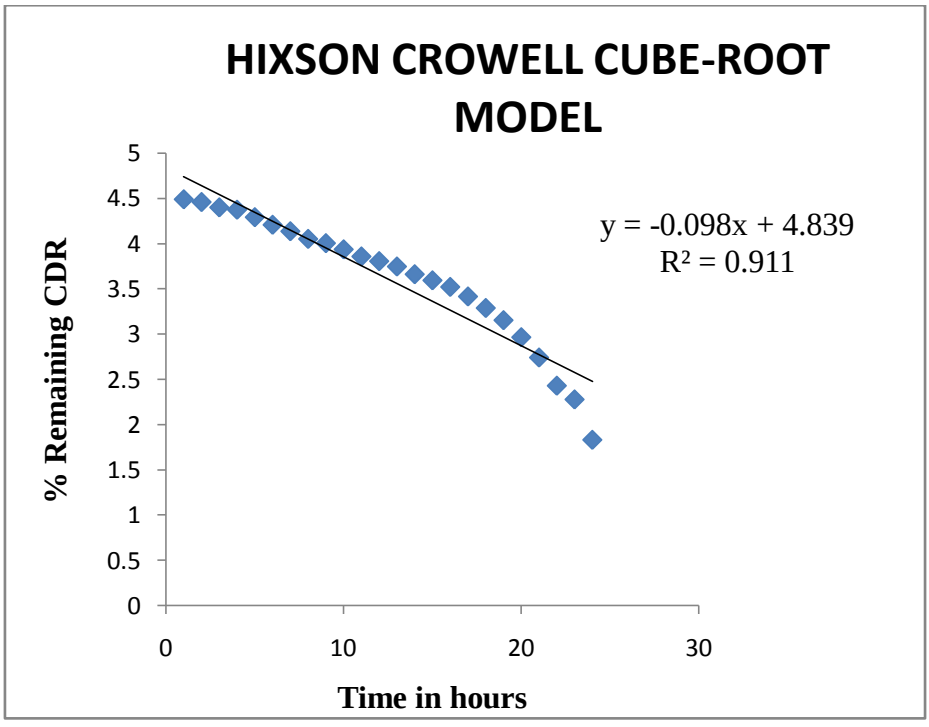
First order kinetics



The release kinetics data indicates that the release of drug from cubosomal capsules best fits to zero order release kinetics because the correlation coefficient values are higher in case of zero order equation. That is release rate is independent of the concentration of the drug.



Higuchi model



Hixson Crowell model

The data obtained from *in-vitro* dissolution studies were also plotted in different kinetic models to find out the mechanism of drug release from the formulation. Higuchi and Hixson Crowell models (corresponding to Diffusion mechanism of release and dissolution mechanism respectively) were plotted to find out the mechanism of release of drug from the dosage form. The data indicated that the R^2 value obtained was found to be greater for Higuchi model. ie the mechanism was found to be diffusion.

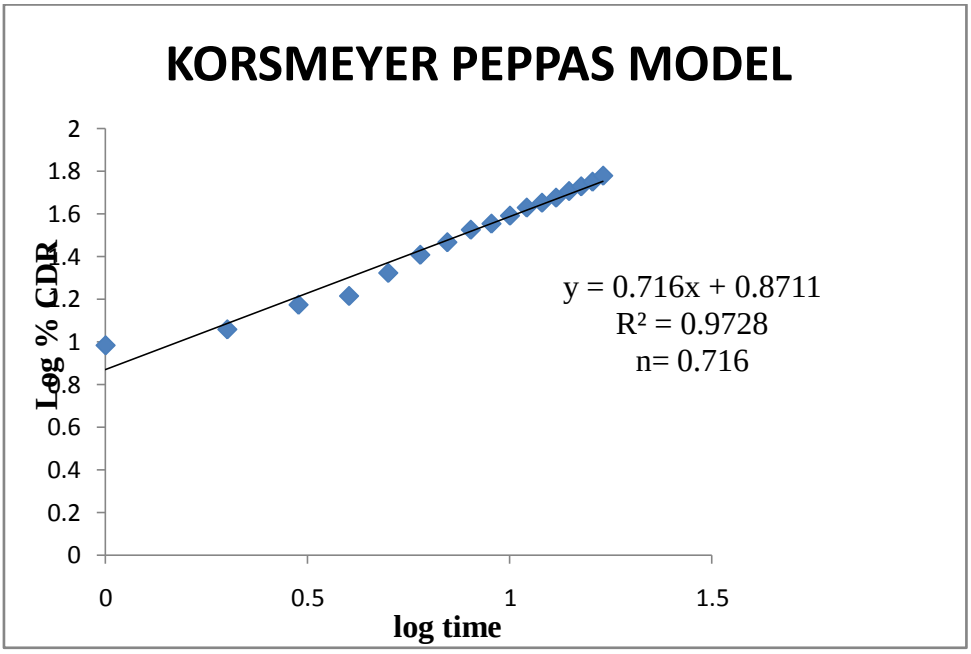
Regression co-efficient (R^2) values of kinetic models for cubosomal capsules

Formulation	R^2 Values			
	Zero order	First order	Higuchi	Hixson Crowell
Cubosomal capsules	0.9917	0.8452	0.9445	0.9115

Since R^2 value of zero order is greater it indicate more linearity, the cubosomal capsules show zero order kinetics. Similarly greater R^2 value for Higuchi model indicates the release mechanism best fits to Higuchi model.

Determination of mechanism of release from Diffusion exponent (*n*)

A plot of log (time) Vs log (%CDR) yields slope *n*, i.e. Diffusion exponent.



Korsemeyer Peppas model

Mechanism of drug release from cubosomal capsules

Formulation code	Release exponent (n)	Drug transport mechanism
Capsules with F_6	0.716	Anomalous (Non Fickian) transport

The value of diffusion exponent,(n) for cubosomal capsule was found to be 0.716, indicates *Anomalous non-Fickian diffusion* of drug cubosomal capsules. The mechanism indicates that the drug release is independent of concentration.

Stability studies

Conditions	Time in days	Drug content	% Drug release
At 40˚C/75%±5%	0	93.03	94.29
	30	92.96	93.84
	60	91.37	91.34
	90	89.82	88.80

CONCLUSION

The aim of the present research work was to enhance the bioavailability of a poorly soluble antiulcerative agent by formulating cubosomes and to convert the cubosomal dispersion to granules and then to capsules.

From the study, it is concluded that, cubosomal dispersion of Omeprazole can be prepared by isotropic dilution method and can be converted into stable capsules. Cubosomes appeared to be an interesting approach to improve problems associated with oral absorption of Omeprazole. The study demonstrates that Cubosome approach may be useful for enhancement of dissolution and ultimately bioavailability of Omeprazole.

The work can be further extended to *in-vivo* analysis and clinical studies. The fruitful resolution of the above mentioned technological suggestions results in a superior oral dosage form of Omeprazole cubosomal capsules.

REFERENCES

1. Sudhakararao GV, Sujana K, Pedababu T. Development and validation of uv spectrophotometric method for the estimation of omeprazole in bulk and pharmacutical formulation, International Journal Of Pharmacy. 2014; 4(1): 247-251
2. Indian pharmacopoeia 2014, vol. I,pp 528
3. Indian pharmacopoeia 2014. Vol. I, pp. 193

4. Spicer PT, Lynch ML, Hoath SB, Visscher MO. Bicontinuous Cubic Liquid Crystalline Phase and CubosomePersonal Care Delivery Systems. Pp. 22.
5. Khalifa MKA. Miconazole Nitrate based cubosome hydrogels for topical application. International Journal of Drug Delivery. 2015; 7, 01-12.
6. Morsi NM, Abdelbary GA , Ahmed MA. Silver sulfadiazine based cubosome hydrogels for topical treatment of burns. European Journal of Pharmaceutics and Biopharmaceutics. 2014; 86 : 178–189.
7. Indira S, Venkatesh B, Srinivas P. Formulation and evaluation of miconazole nitrate as a cubosomal topical gel. Journal of Global Trends in Pharmaceutical Sciences. 2014;5(4), 2037-2047.
8. Yallappamaharaj R, Hundekar, Saboji JK, Patil SM, Nanjwade BK. Preparation and evaluation of diclofenac sodium cubosomes for percutaneous administration. World journal of pharmacy and pharmaceutical sciences. 2014; 3(5), 523-539.
9. Bhargavi K, Indira S, Srinivas P. Formulation and evaluation of aceclofenac cubosomal oral capsules. World journal of pharmacy and pharmaceutical sciences. 4(11), 1167-1181.
10. B.Venkatesh, S.Indira, Srinivas P. Formulation and Evaluation of Glimepiride Oral Capsules. International Journal of Pharmaceutical Science Invention. 2014; 3(10):01-13.
11. Subrahmanyam CVS, Thimmasetty J. Laboratory Manual of Physical Pharmaceutics. 28
12. Indian pharmacopoeia 2014, vol. I,pp 256
13. Indian pharmacopoeia 2014, vol. I,pp 253
14. Shaikh HK, Kshirsagar RV, Patil SG. Mathematical models for drug release characterization: a review. World Journal off pharmacy and pharmaceutical sciences.2015; 4(4):324-338
15. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta poloniae pharmaceutica n drug research. 2010;67(3):217-223
16. Singhvi G, Singh M. Review: *in-vitro* drug release characterization models. International Journal of Pharmaceutical Studies and Research.2011;2(1):77-84
17. Indian pharmacopoeia 2014, vol. I,pp. 528.