ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 3, Issue 31, August, 2015, 41-61

Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF SUSTAINED RELEASE OXCARBAZEPINE TABLET

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Received 27 July 2015; Accepted 10 August 2015

ABSTRACT

The Sustained release drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose, to individualize treatment more effectively. Oxcarbazepine indicated as monotherapy or adjunctive therapy for the treatment of partial seizures with or without secondarily generalized tonic-clonic seizures in adults and children. The polymer hydroxy propyl methyl cellulose (HPMC) was selected. The other excipients were used are magnesium stearate used as lubricant, Polyvinylpyrrolidone used as binder of tablet, and cross carmellose sodium as super disintegration agent. Oxcarbazepine was prepared by wet granulation technique.

FTIR was done to show there was no drug interaction with formulation additive to tablet.

The pre-compression study indicated the excellent flow properties of bulk powder which is within acceptable range according to pharmacopeia specifications.

The post-compression parameters results match the expected criteria specifications.

The Cumulative %Drug release of formulation F9 showed the highest release 98.34%. Formulation F1, F2, F3, F4,F5,F6,F7,F8 showed 68.35,78.33,88.77,85.39,88.46,90.46,92.88 & 89.65 in 12 hours.The stability study of the prepared tablets were carried out according to ICH guidelines at 2±2^{0}C, 25±2^{0}C/60±5% RH, 30±2^{0}C/65±5% RH, 40±2^{0}C/75±5% RH, 55±2^{0}C for one month by storing the samples in stability chamber.

Key Words: Oxcarbazepine, Hydroxy Propyl Methyl Cellulose, MagnesiumStearate, Cross Carmellose Sodium.

1. INTRODUCTION

In recent years, the number of commercially available antiepileptic drugs (AEDs) has increased steadily. Although this may complicate management choices, it also offers welcome new options to individualize treatment more effectively. Because each of the available AEDs differs from others in many clinically relevant properties, opportunities to tailor drug treatment to the characteristics of the individual patient have never been greater. Properties that are especially important in drug selection in patients with epilepsy include spectrum of efficacy in different seizure types, adverse effects profile, pharmacokinetic properties, susceptibility to cause or be a target of clinically important Antiepileptic drugs are medicines that reduce the frequency of epileptic .This class of drugs include some drugs that have other uses as well. Phenobarbital is a barbiturate. Barbiturates were once widely used as sleeping pills and are still used in anesthesia for surgery. Clonazepam, clorazepate, and diazepam are members of the benzodiazepine group of drugs and are best known for their use as tranquilizers.Oxcarbazepine (10, 11-dihydro-10-oxo-5H-dibenzazepine-5-carboxamide) is an antiepileptic drug registered worldwide by Novartis under the trade name Trileptal®. Trileptal® is approved as adjunctive therapy or monotherapy for the treatment of partial seizures in adults and in children. In the US, Trileptal® is approved as adjunctive therapy in adults and in children ≥4 years of age and as monotherapy in adults and in children. Trileptal is currently marketed as 150, 300 and 600mg film-coated tablets for oral administration. A 60 mg/mL (6%) oral suspension formulation has also been registered world-wide. Oxcarbazepineand its pharmacologically active metabolite, 10-monohydroxy derivative (MHD; 10, 11-dihydro-10-hydro-carbamazepine) show potent antiepileptic activity in animal models comparable to that of carbamazepine and phenytoin. Oxcarbazepine and MHD have been shown to exert antiepileptic activity by blockade of voltage-dependent sodium channels in the brain.

2. Materials and methods

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The following analytical-grade reagents were used: Oxcarbazepine (Lucid Colloids Ltd), sodium lauryl sulfate and 0.1% HCL (Institute laboratory), Lactose and Methyl Paraben (Signet Chemical Corporation Mumbai), H.P.M.C K100M and Iso propyl alcohol (Lucid Colloids Ltd India.),Talcum(Udaipur minerals development syndicate Pvt. Ltd.), PVPK-30 (Colorcon Asia Pvt.Ltd Verna-Goa).

Oxcarbazepine was prepared by wet granulation technique.*All raw material & excipients were passed through a #40 Separately*, OXZ, Polymer&Lactose were mixed. PVP paste was made by adding IPA.PVP paste was thoroughly mixed with the mixtue of polymers & drugs. Mixing product was passed through the #20. Granules were dried at 40˚c in an oven dryer for 30 minutes. Then granules were coated with methacrylicacid . Then again leave for dry in an oven dryer. Granules thus formed were passed through #18.Granules mixed with, colloidal silicon dioxide, magnesium stearate & talcum. Then compression was done.

Table 1: Formulation of Sustained released Oxcarbazepine tablet(300 mg.)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Oxcarbazepine	300	300	300	300	300	300	300	300	300
HPMCK100M					35	50	60	65	70
Cross carmellose sodium	8.39	8.39	8.39	8.39	10.21	10.21	10.21	15.01	13.33
Collodial silicon dioxide	3.33	3.33	3.33	3.33	3.33	3.33	3.33	3.33	3.33
PVPK30	4.36	4.36	4.28	6.42	6.42	7.14	7.14	8.33	8.33
Purified talc	4	4	4	4	4	4	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Lactose	215.92	185.92	184.99	185.86	156.04	156.32	156.32	156.40	160.01

Methyl Paraben and iso propyl alcohol added in each formulation

Coating agent – Methacrylic acid copolymer

Coating solution – Iso propyl alcohol

Methods

1. Tablet Thickness

Thickness of tablets is important for uniformity of tablet size .thickness can measured using digital vernier caliper. Five tablets from each batch are used, and average value calculated.

2. Weight of variation

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance, and the average weight was determined for each formulation. Test was performed according to the official method. Not more than two of the individuals' weights deviate from the average weight by more than the percentage shown in the table and non-deviates by more than twice that percentage.

Table 1: Specifications for Tablet Weight variation as per Indian Pharmacopoeia

Average Weight of Tablet	% Deviation
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 mg or more	5

3. Hardness:-

Tablet hardness testing is also called tablet breaking force testing. For this test the tablets are placed between two plates. One of the plates moves in order to damage the tablet. The breaking force is the force required to break or damage the tablets in a specific plane. Tablet

breaking force measurement is frequently used as an alternative to compression force measurement. This is an essential quality control parameter since compression influences many tablet properties including disintegration, dissolution and friability.

We have hardness tester that can perform your hardness measurements in two modes: constant plate movement or constant loading rate. This equipment is also capable of measuring tablet weight, thickness, width and diameter .The resistance of tablets to shipping or breakage, under condition of storage, transportationand handling before usage depends on its hardness. For each formulation, the hardness of 6tablets was determined using the Monsanto hardness tester .The Tablet was held along itsaxis in between the two jaws of the tester. At this point reading should be zero kg /cm^2.Then constant force was applied by rotating the knob until the tablet fractured. The Valueat this point was noted in kg/cm^2.

4. Friability:

Friability is a measure of the resistance of the tablets to shipping and abrasion by tumbling them in a rotating drum. After tumbling, the integrity of the tablets and the weight loss are evaluated. Anabiotec has a Sotax F1 friability tester. With this equipment it is possible to measure in two modes: a specific time interval or a specified number of rotations. Friability is the measure of tablet strength. Roche Friabilator is used for testing the friability using the following procedure. For each formulation, the friability tablets were determined using the Roche Friabiltaor. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. In this approximately 6gm of the de dusted tablets are subjected to 100 free falls in a rotating drum and are than reweighed. Percent friability (% F) was calculated as follows,

$$\% \text{ friability} = \frac{\text{initial weight} - \text{final weight} * 100}{\text{initial weight}}$$

A loss of less than 1% in weight in generally considered accept

5. Disintegration test

An orally administered drug must disintegrate to attain good absorption of its active substance. The first step toward dissolution is usually the break-up of the tablet; a process described as disintegration. The disintegration test results in a time necessary to disintegrate a group of tablets into small particles under standard conditions. The disintegration test is a valuable tool in quality control environments. The test is used for batch release and trending of lot-to-lot variations during manufacturing of tablets. However, it is not a bioavailability indicator. Anabiotec has a Sotax DT2 disintegration tester at your disposal, allowing both manual and automated disintegration testing on baskets with three or six tubes.

6. Dissolution test –

Dissolution test was carried out using USP type II (paddle) apparatus for 1h. The stirring was kept at 25rpm, 0.75% SLS and 0.1N HCl as a dissolution medium (900mL) for OXC and temperature was maintained at 37 ± 1ºC. 5mL of samples were collected at regular time intervals of 0, 5, 10, 15, 20, 30, 45 and 60min and were assayed spectrophotometically at 256nm for OXC with a triplicate number of experiments was performed.

Model dependent methods

Model dependent methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected, the dissolution profiles are evaluated depending on the derived model parameters.

The model dependent approaches included

(1) Zero Order Model
(2) First Order Model
(3) Higuchi Model
(4) Korsmeyer-Peppas Model

(1) Zero order model

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$Q_0 - Q_t = K_0 t$

Rearrangement of equation yields:

$Q_t = Q_0 - K_0 t$

Where, Q_t is the amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution (most times, $Q_0 = 0$) and K0 is the zero order release constant expressed in units of concentration/time. To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time.

Application: This relationship can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as matrix tablets with low soluble drugs in coated forms, osmotic systems, etc.

(2)First-Order model

This model has also been used to describe absorption and/or elimination of some drugs**,** although it is difficult to conceptualize this mechanism on a theoretical basis. The release of the drug which followed first order kinetics can be expressed by the equation:

$dc/dt = -Kc$

where K is first order rate constant expressed in units of time

Equation can be expressed as:

$\log C = \log C_0 - K_t / 2.303$

where, C_0 is the initial concentration of drug, k is the first order rate constant, and t is the time . The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of -K/2.303.

Application: This relationship can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices.

(3) Higuchi model

The first example of a mathematical model aimed to describe drug release from a matrix system was proposed by Huguchi in 1961. Initially conceived for planar systems, it was then extended to different geometrics and porous systems. This model is based on the hypotheses that (i) initial drug concentration in the matrix is much higher than drug solubility; (ii) drug diffusion takes place only in one dimension (edge effect must be negligible); (drug particles are much smaller than system thickness; (iv) matrix swelling and dissolution are negligible; (v) drug diffusivity is constant; and (vi) perfect sink conditions are always attained in the release environment. Accordingly, model expression is given by the equation:

$f_t = Q = A \sqrt{D(2C - Cs) Cs t}$

Where Q is the amount of drug released in time t per unit area A, C is the drug initial concentration, Cs is the drug solubility in the matrix media and D is the diffusivity of the drug molecules (diffusion coefficient) in the matrix substance. This relation is valid during all the time, except when the total depletion of the drug in the therapeutic system is achieved. To study the dissolution from a planar heterogeneous matrix system, where the drug concentration in the matrix is lower than its solubility and the release occurs through pores in the matrix.

(4) Korsmeyer and Peppas Model

Korsmeyer et al. (1983) derived a simple relationship which described drug release from a polymeric system .To find out the mechanism of drug release, first 60% drug release data were fitted in KorsmeyerPeppas model .

$M_t / M_\infty = K^{t/n}$

Where, M_t / M_∞ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent. The n value is used to characterize different release for cylindrical shaped matrices. In this model, the value of n characterizes the release mechanism of drug as described in Table 1. For the case of cylindrical tablets, $0.45 \leq n$ corresponds to a Fickian diffusion mechanism, $0.45 < n < 0.89$ to non Fickian transport, n = 0.89 to Case II (relaxational) transport, and $n > 0.89$ to super case II transport (37, 38).To find out the exponent of n the portion of the release curve, where $M_t / M_\infty < 0.6$ should only be used. To study the release kinetics, data obtained from in vitro drug release studies were plotted as log cumulative percentage drug release versus log time.

Microbiological identification test –

(1) Escherichia coli –

Using casein soyabean digest broth (medium 1) as a diluent make 1 in 10 dilution of more than 1 gram of the product as mentioned. Under total aerobic viable count in microbial contamination in non sterile products and use 10 ml or the quantity corresponding to 1 gram or 1 ml of the product to inoculate a suitable amount of soyabean digest broth , incubate 30^0 to 35^0 for 18 to 24 hours.

After incubation shake the broth and transfer 1 ml to 100 ml of Macconkey broth (Medium) incubate at 42^0 to 44^0 For 24 to 48 hours. Subculture on a plate of Macconkey agar (Medium8) and incubate at 30^0 to 35^0 for 18 to 72 hours. Growth of pink, nonmucoid colonies indicated the possible presence of Escherichia coli.

No growth of such type of colonies, or the identification tests are negative it's indicate absence of e.coli and the products passes the test.

(2) Salmonella –

Prepare a sample from the product. Total aerobic viable count in microbial contamination in nonsterile products and use the quantry corresponding to 10 gram or 10 ml of the products to inoculate a suitable amount of casein soyabean digest broth incubate at 30^0 to 35^0 for 18 to 24 hours. After incubation shake the broth and transfer 0.1 mi to 10 ml of rappapartvassilicides salmonella enrichment broth (medium 9) and incubate at 30^0 to 35^0 for 24 to 48 hours. Subculture on a plate of Wilson and Blair's BBS agar (medium 10) and incubate 30^0 to 35^0 for 24 to 48 hours. Green colonies with black centre develop and in 48 hour the colonies become uniformity black. Colonies surround by a dark jone and metallic seen indicates possibility presence of salmonella.

If subcultured on plates of xylose, lysine deoxycholate agar and incubated at 30^0 to 35^0 for 24 to 48 hours. Well developed red colonies with or without black centers indicates possibility of salmonella.

This should be confirmed by identification tests. Negative its indicates absence of salmonella and the product passes the test.

(3) Pseudomonas aeruginosa –

Using casein soyabean digest broth as a diluent make 1 in 10 diluent of more than 1 gram of the product mentioned

in total aerobic viable count under microbial contamination in nonsterile products and use 10 ml or the quantity corresponding to 1 gram or 1 ml of the product inoculate a suitable amount (determine as under validity of the test method) of casein soyabean digest broth incubate at 30^0 to 35^0 incubate for 18 to 24 hours.
Subculture on a plate of Cetrimide agar (medium 13) and incubate at 30^0 to 35^0 for 18 to 24 hours. A greenish color colony indicates the possibility of presence of pseudomonas aeruginosa. This should be confirmed by identification test .
If there is no growth of such types of colonies or identification tests are negative its indicates absence of P.aeruginosa and the product passes the test.

(4) Staphylococcus aureus –

Using casein soyabean digest broth as a diluent make 1 in 10 diluent of more than 1 gram of the product mentioned in total aerobic viable count under microbial contamination in nonsterile products and use 10 ml or the quantity corresponding to 1 gram or 1 ml of the product inoculate a suitable amount (determine as under validity of the test method) of casein soyabean digest broth incubate at 30^0 to 35^0 incubate for 18 to 24 hours.
Subculture on a plate of mannitol agar (medium 13) and incubate at 30^0 to 35^0 for 18 to 72 hours. Yellow or white colonies indicate the possibility of presence of S. aureus. This should be confirmed by identification tests.
No growth of such type of colonies or the identification tests or negative its indicates absence of S.aureus and the products passes the test.

Stability Studies and Storage Condition –

To check the effect of environmental condition or storage condition on formulation Optimized batch was kept in environmental stability chamber for accelerated stability condition at 40 ^{0} C temperatures and 75 ± 5 % relative humidity. The samples were withdrawn at 1 month interval and evaluated for physical parameters, drug content and in vitro drug release.

Table 2: ICH guidelines for stability study.

Conditions	Temperature	Duration
Freezer condition	-20˚to -10˚c	_
Refrigerator	2˚to8˚c	_
Controlled room temperature	15˚to30˚c	Till expiry date
Accelerated temperature	40˚to50˚c	6months

3.Result and discussion

PREFORMULATION STUDIES:-

Preformulation studies are the first step in the rational development of dosage form of a drug substance.

1. Organoleptic Properties:-

It is an initial method to identify the powder by sensory organs. Following are the specification of oxcarbazepine powder**.**

Table 3: organoleptic properties of oxcarbazepine

Properties	**Results**
Description	amorphous
Color	Off-white to yellow
Odor	odorless
Taste	bitter

2. Loss on Drying:-

According to I.P, it should not more than 0.5%.

Weight of blank apparatus=89.0342gm
Weight of sample in apparatus=90.0819gm
So weight of sample= (90.0819-89.0342) gm.
=1.0477gm
% of loss on drying= 0.0032×100/1.0477
=0.3054%

3. Sulphated Ash:-

According to I.P it should not more than 0.1%.
Weight of crucible=20.0245gm
Weight of sample=01.000gm
Total weight=21.0245gm
Then add H_2SO_4, to wet the sample then keep for 1 hour to ignite in muffle furnace.
Weight after ignite=20.0249gm
So, amount of residue=(20.0249-20.0245)gm.
=00.0004gm
%of sulfated ash=00.0004gm×100\01.000gm
=0.07%

4. Melting Point Test:

Table 4: Observation of melting point

Observed	reported
215˚c-217˚c	216˚c

5. Solubility:-

Table 5: solubility in different reagents

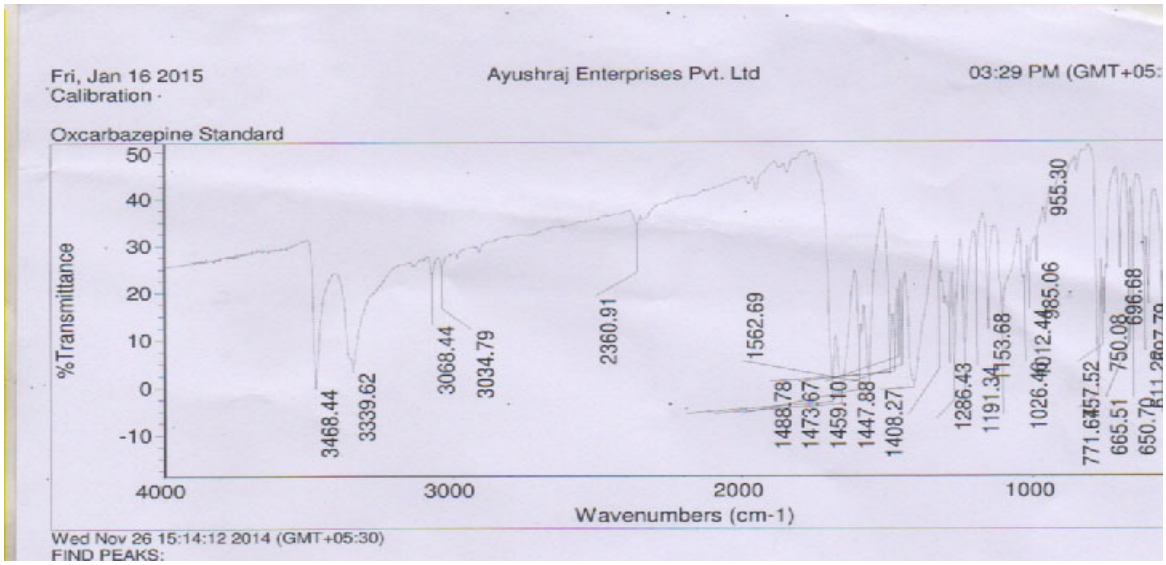
Reagents	solubility
Acetic acid	Soluble
Chloroform	Sparingly soluble
Water	Practically insoluble

Solubility test:

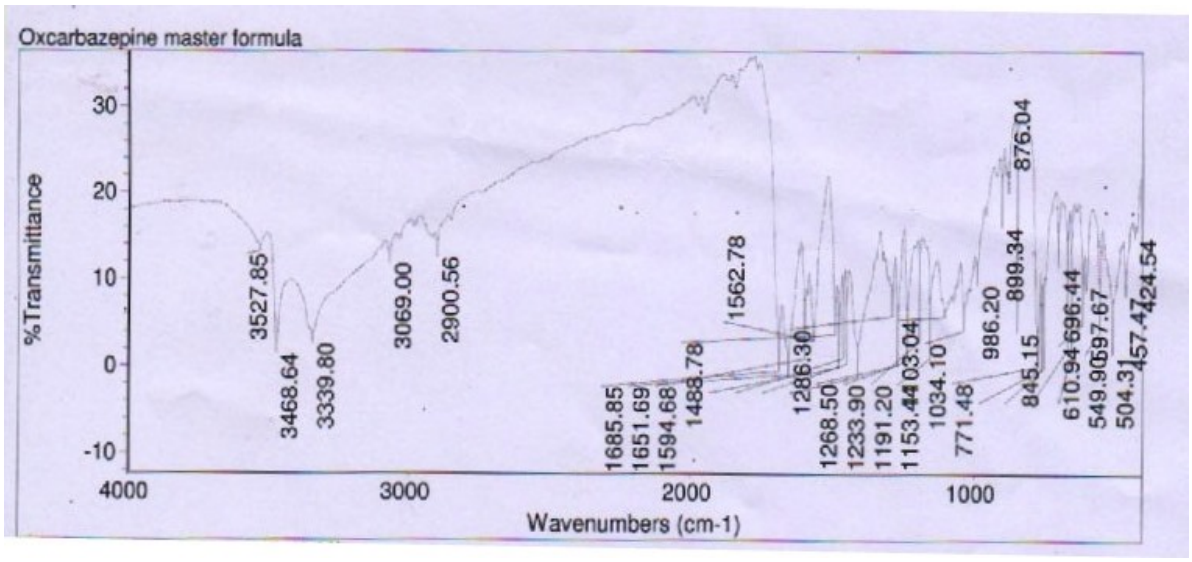
solvents	**solubility**
Water	Practically insoluble
pH 6.8 phosphate buffer	Slightly soluble
0.1 N HCL	soluble
0.1 N HCL with SLS	More soluble

FTIR

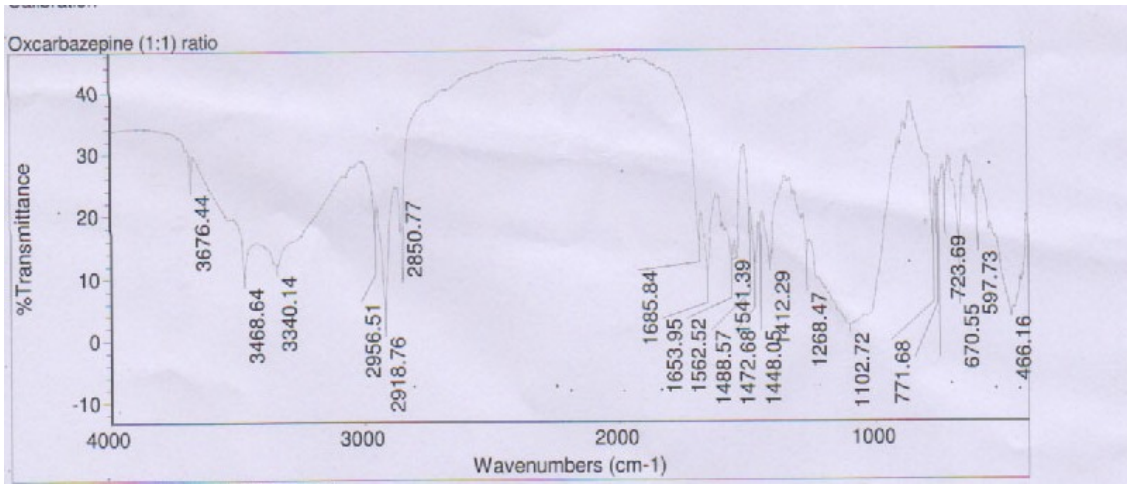
1 Standard of oxcarbazepine:



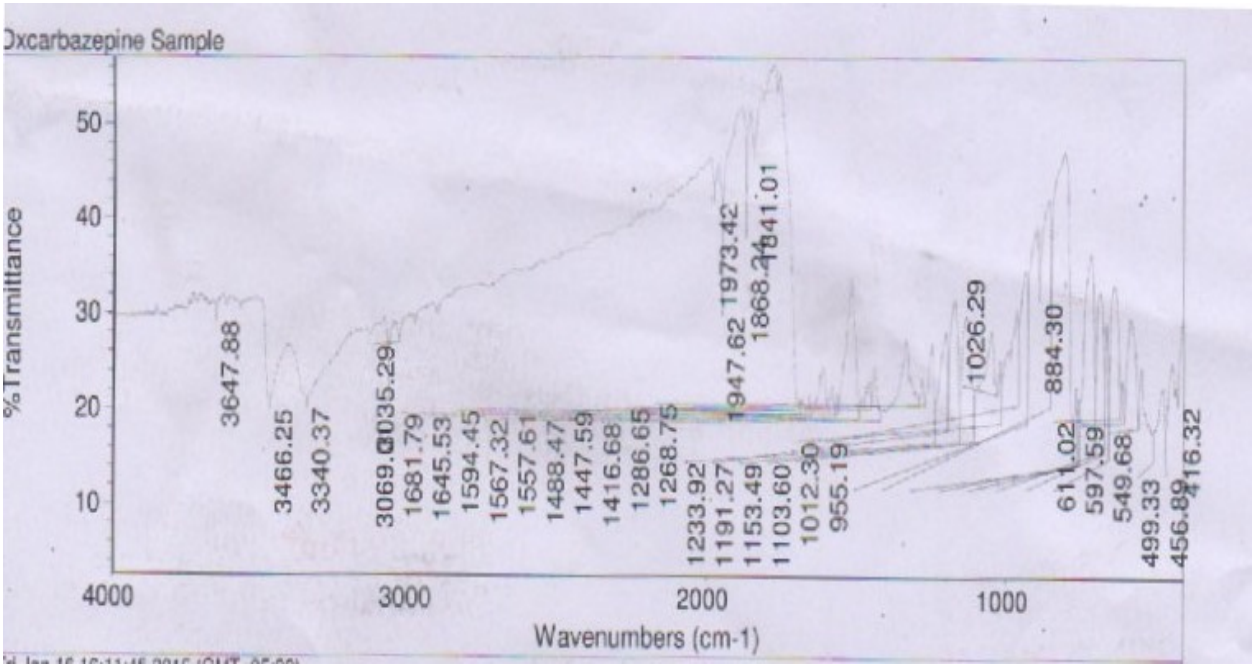
2 Master formula of oxcarbazepine:



3 Oxcarbazepine in 1:1 ratio:

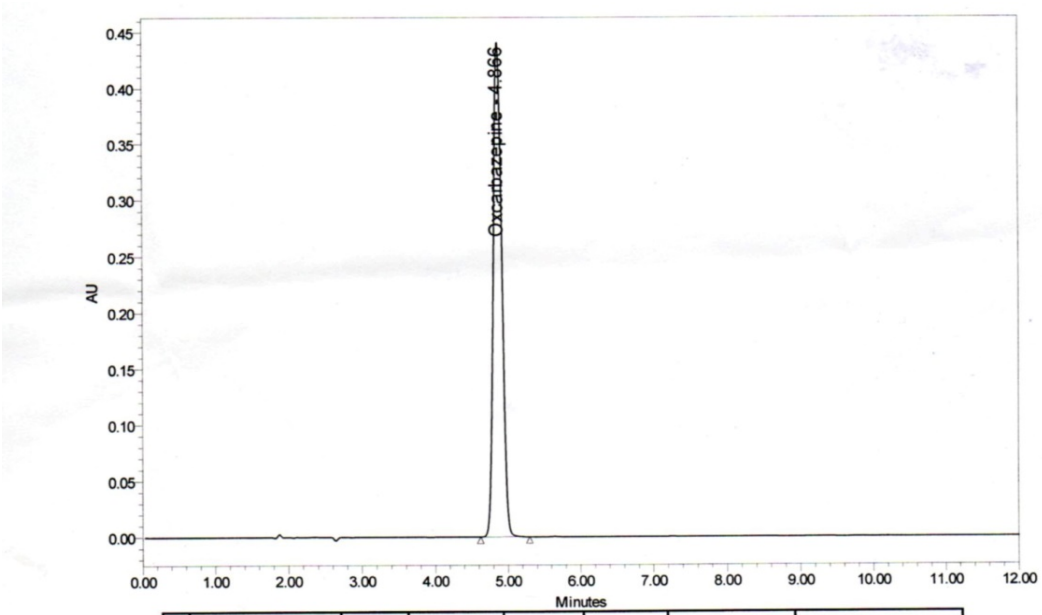


4 Sample of oxcarbazepine:



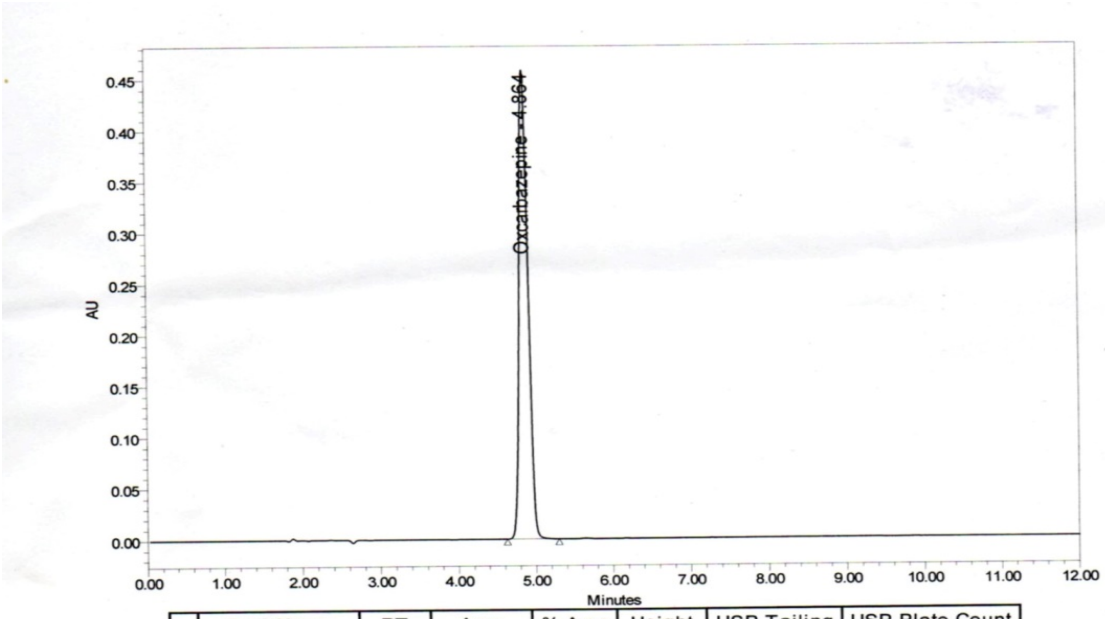
H.P.L.C

1Sample of oxcarbazepine



	Peak Name	RT	Area	% Area	Height	USP Tailing	USP Plate Count
1	Oxcarbazepine	4.866	3593180	100.00	440911	1.1	8031

2 Standard of oxcarbazepine



	Peak Name	RT	Area	% Area	Height	USP Tailing	USP Plate Count
1	Oxcarbazepine	4.864	3688382	100.00	458426	1.1	8266

Table 6: Range of functional group

IR PEAK(wave length cm^{-1})	**FUNCTIONAL GROUP**
3200-3550	OH group

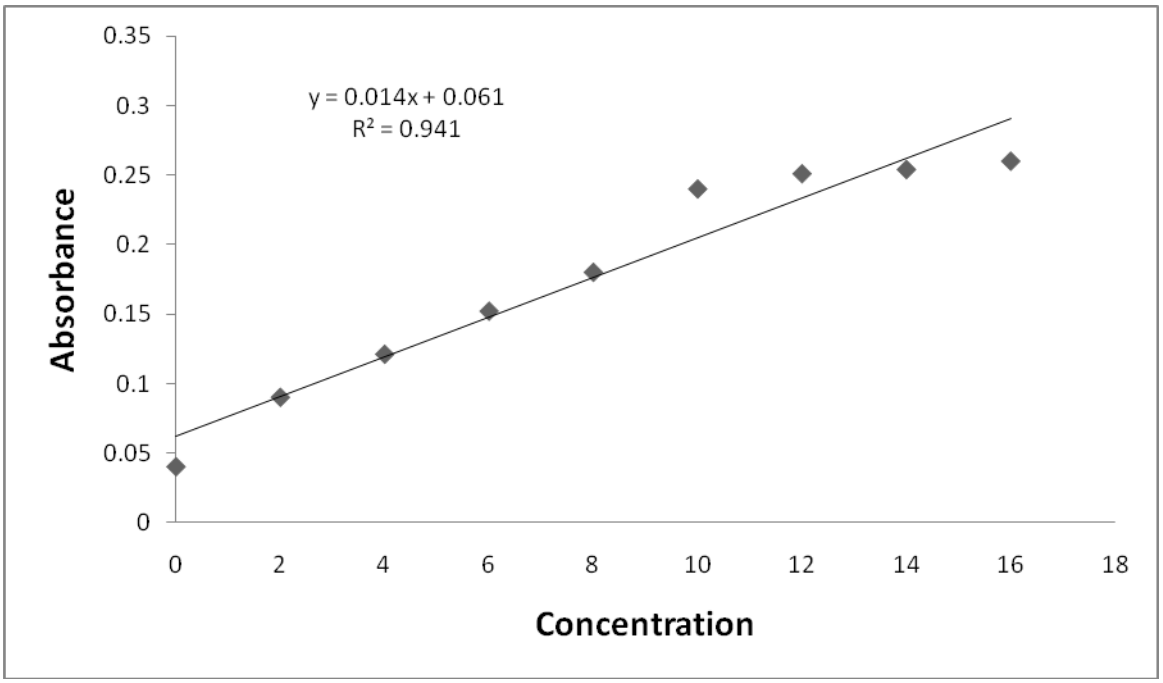
3400-3500	N-H group
1759-1680	Ketone group
1219-1320	Carboxylic group

Table 7: Drug compatibility study

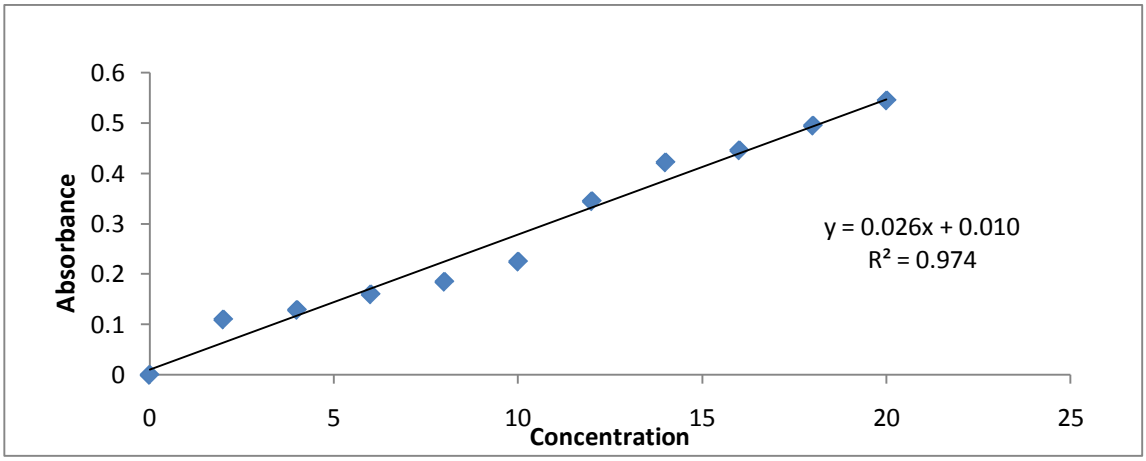
S. No.	Drug +Excipient	Category	Initial	Stability(40^0 c/75%RH	Comments
1.	Oxcarbazepine	Active ingredient	white	No change	Compatible
2.	Oxcarbazepine+ Cross carmellose sodium	Super disintegration	white	No change	Compatible
3.	Oxcarbazepine +Colloidal silicon dioxide	Glidant	white	No change	Compatible
4.	Oxcarbazepine + P.V.P.K 30	Binder	white	No change	Compatible
5.	Oxcrazepine+HPMCK100M	Binder	white	No change	Compatible
6.	Oxcarbazepine +Purified talc	Glidant	white	No change	Compatible
7.	Oxcarbazepine +Magnesium stearate	Lubricant	white	No change	Compatible
8..	Oxcarbazepine Lactose	Filler	white	No change	Compatible
9.	Oxcarbazepine +Methyl Paraben	Preservative	white	No change	Compatible

Table 8: Calibration Data of oxcarbazepine in phosphate buffer of pH1.2 & 6.8

S.N.	**Concentration(µg/ml)**	**Absorbance at 254nm for acidic buffer of pH 1.2**	**Absorbance at 254nm for phosphate buffer of pH 6.8**
1.	0	0.00	0.00
2.	2	0.04	0.11
3.	4	0.9	0.129
4.	6	0.121	0.160
5.	8	0.152	0.185
6.	10	0.180	0.225
7.	12	0.240	0.345
8.	14	0.251	0.422
9.	16	0.254	0.446
10	18	0.260	0.495
11.	20	0.284	0.545



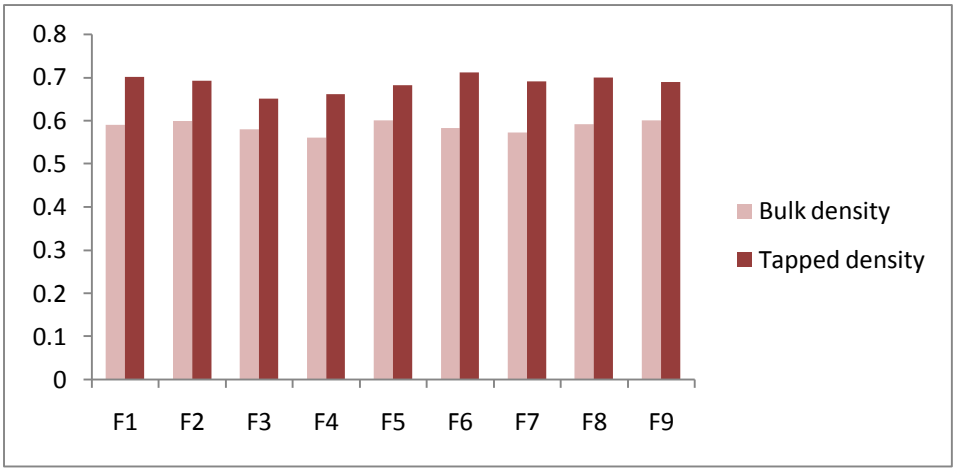
Standard Calibration Curve of oxcarbazepne in acidic buffer of 1.2



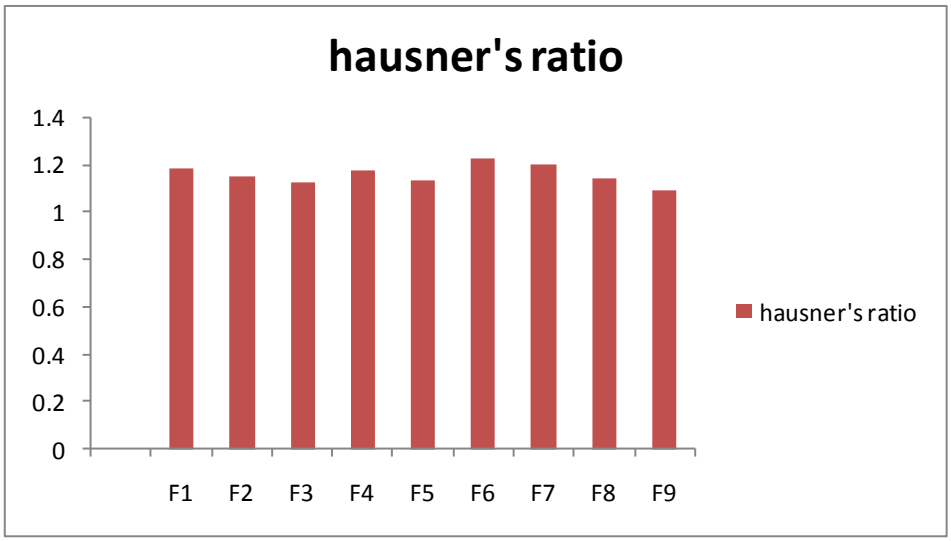
Standard Calibration Curve of Oxcarbazepine in Phosphate buffer of pH 6.8.

Table 9: Evaluation of powder blends

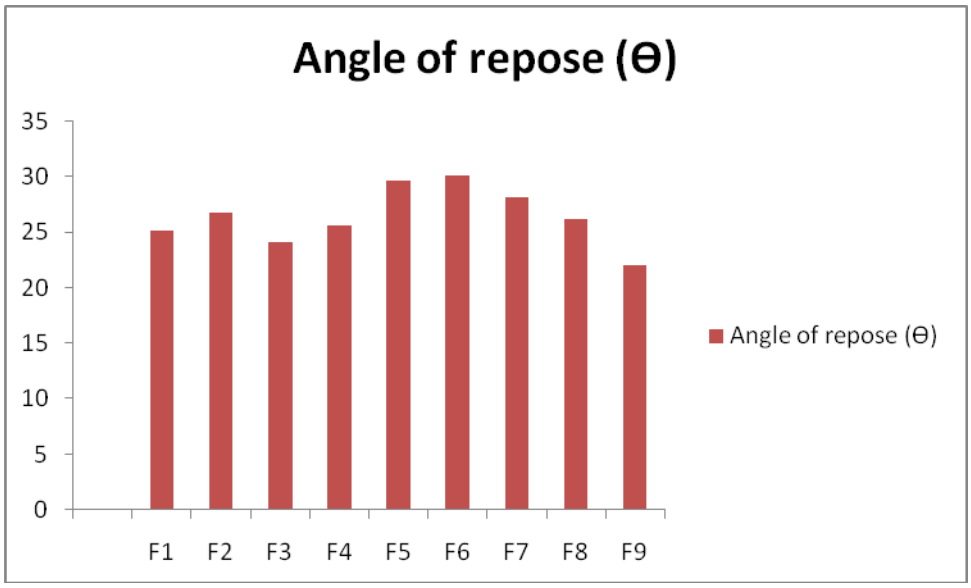
Formulation	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Hausner's Ratio	Angle of Repose (ɵ)	Carr"s Compressibility Index (%)
F1	0.590±0.004	0.701±0.015	1.18	25.22	15.83
F2	0.599±0.005	0.692±0.009	1.15	26.77	13.43
F3	0.580±0.002	0.651±0.019	1.12	24.11	10.90
F4	0.561±0.006	0.661±0.014	1.17	25.66	15.12
F5	0.601±0.002	0.682±0.019	1.13	29.72	11.87
F6	0.582±0.003	0.712±0.021	1.22	30.12	12.28
F7	0.572±0.002	0.690±0.018	1.20	28.23	17.10
F8	0.600±0.004	0.689±0.009	1.14	26.22	12.09
F9	0.592±0.004	0.650±0.012	1.09	22.12	08.90



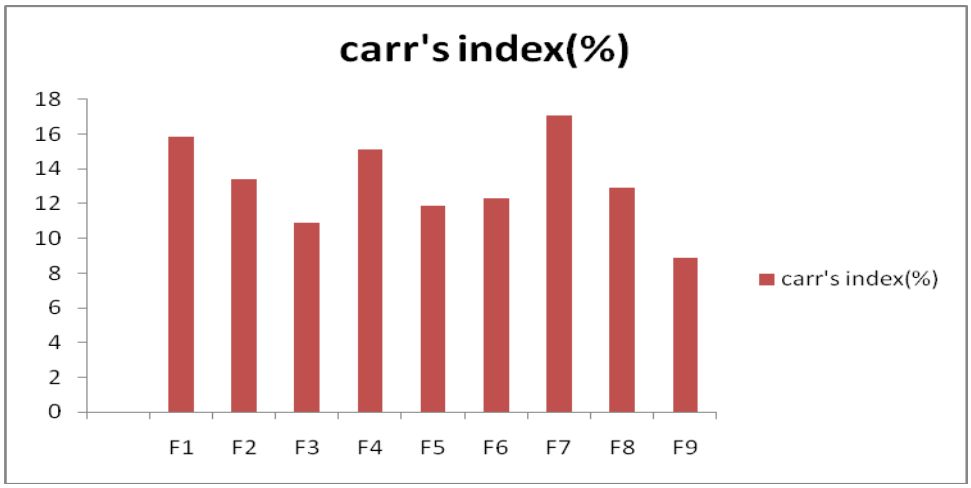
Graph showing Bulk Density and Tapped Density of various formulations



Graph showing Hausner´ Ratio of various formulation



Graph showing angle of repose of various formulation



Graph showing carr's index of various formulation .

Table 10: Post compression evaluation of sustained release tablet of Oxcarbazepine

Formulation	Shape	Color	Average Weight of 20 Tablets (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	% Drug Content
F1	Round	white	541.9	6.2	8.12	0.212	97.365
F2	Round	white	541.6	6.4	7.22	0.446	98.649
F3	Round	white	543.5	6.7	8.20	0.129	97.094
F4	Round	white	545.8	6.0	7.25	0.554	99.182
F5	Round	white	545.3	6.6	7.96	0.467	98.468
F6	Round	white	555.6	6.9	7.88	0.672	99.648
F7	Round	white	541.9	6.	8.12	0.832	98.450

				2			
F8	Round	white	550.9	6.4	8.23	0.421	99.591
F9	Round	white	544.2	6.4	7.99	0.356	99.912

FORMULA USED IN CALCULATIONS

Concentration of drug (µg/ml) = (slope × absorbance) ± intercept

Amount of drug = $\frac{\text{Concentration} \times \text{Dissolution bath volume} \times \text{dilution factor released mg/ ml}}{1000}$

Cumulative percentage Release (%)

=Volume of sample withdrawn (ml) × P (t – 1) + Pt release (%) Bath volume(V)

Where,Pt = Percentage release at time t , P (t – 1) = Percentage release previous to 't'

Dissolution Formulation

$$\frac{\text{Absorption of sample Peak}}{\text{Absorption of standard Peak}} \times \frac{\text{dilution of standard}}{\text{dilution of test}} \times 1 \times \text{Potency Factor} \times \text{Average Weight}$$

Table 11: Cumulative %Drug release

Time (hrs)	Cumulative %Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	1.14	3.22	5.16	5.42	1.22	1.82	2.33	5.51	6.13
2	3.25	2.2	9.3	8.21	11.19	6.12	8.30	6.71	9.31
3	5	15.12	14.12	9.22	3.21	6.12	10.12	14.33	16.22
4	12.21	18.11	21.33	10.11	9.97	15.22	22.34	18.56	28.43
5	14.71	21.22	22.77	25.37	28.12	30.85	35.99	38.21	39.41
6	16.52	22.18	24.15	26.76	36.87	39.68	42.77	43.66	44.28
7	20.12	27.44	29.14	30.18	32.76	35.98	46.88	55.98	59.88
8	26.22	29.66	35.77	39.87	40.86	42.88	50.67	69.35	64.55
9	30.29	42.66	48.55	45.67	48.99	57.78	64.98	78.00	77.23
0	41.42	55.15	59.25	62.97	69.27	75.87	71.57	80.25	85.10
1	55.23	63.77	68.92	70.48	75.48	84.95	86.99	86.46	88.98
2	68.35	78.33	80.77	85.39	88.46	90.46	92.88	89.65	98.34

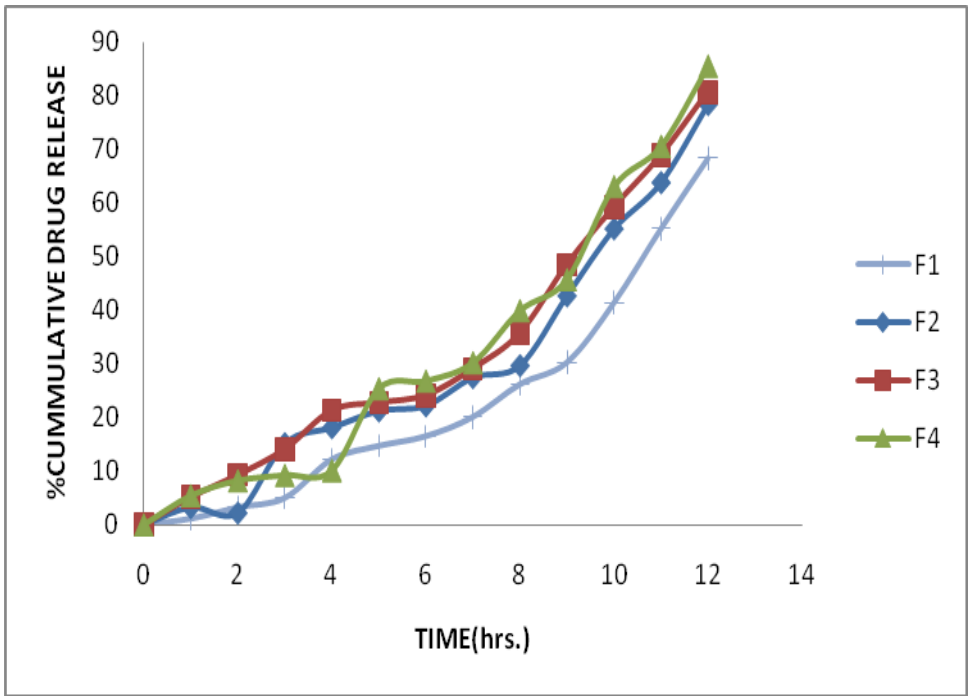


Figure i: Dissolution study of oxcarbazepine (F_1 to F_4)

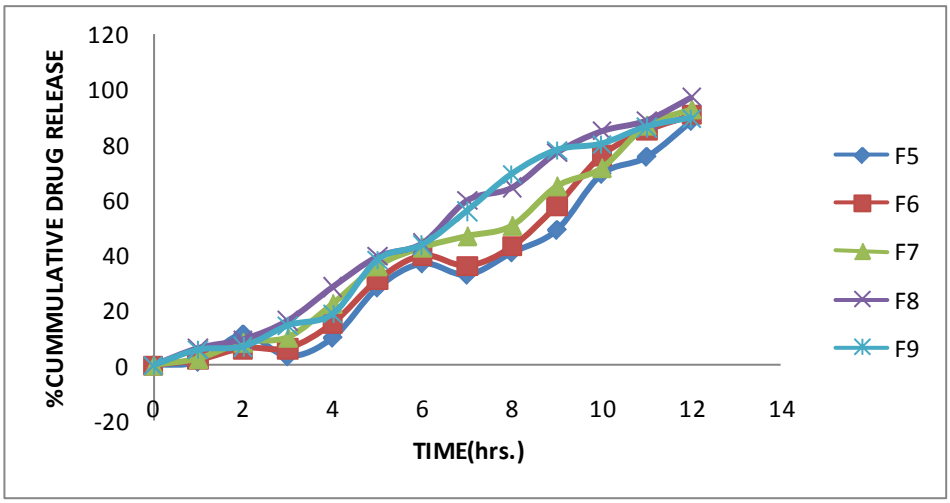


Figure ii:Dissolution study of oxcarbazepine (F_5 to F_9)

Table 12: Comparison of the slope and the regression co-efficient for different models for optimized formulation F9

Time (hrs)	SQRT (Square root)	Log Time	%CDR	Log% CDR	%Drug Retained (100 -%CDR)	Log% Drug Retained	%Drug Retained$^{1/3}$
0	0	0	0	0	0	0	0
1	1	0	6.13	0.7874	93.87	1.9725	4.54
2	1.41	0.3010	9.31	0.9689	90.69	1.9575	4.49
3	1.73	0.4771	16.22	1.2100	83.78	1.9231	4.37
4	2.00	0.6020	28.43	1.4537	71.57	1.8547	4.15
5	2.23	0.6989	39.41	1.5956	60.59	1.7824	3.92

6	2.44	0.7781	44.28	1.6462	55.72	1.7460	3.81
7	2.64	0.8450	59.88	1.7772	40.12	1.6033	3.42
8	2.82	0.9030	64.55	1.8098	35.45	1.5496	3.28
9	3.00	0.9542	77.23	1.8877	22.77	1.3573	2.83
10	3.16	1.0000	85.10	1.9299	14.09	1.1731	2.46
11	3.31	1.0413	88.98	1.9492	11.02	1.0421	2.22
12	3.46	1.0791	98.34	1.9882	2.66	0.4248	1.38

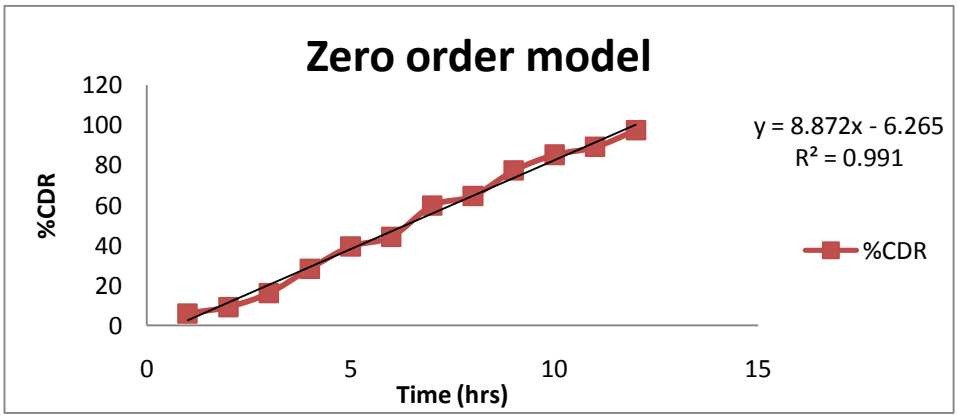


Figure iii: In vitro release profile of Oxcarbazepine for zero order release kinetics for optimized formulation F9

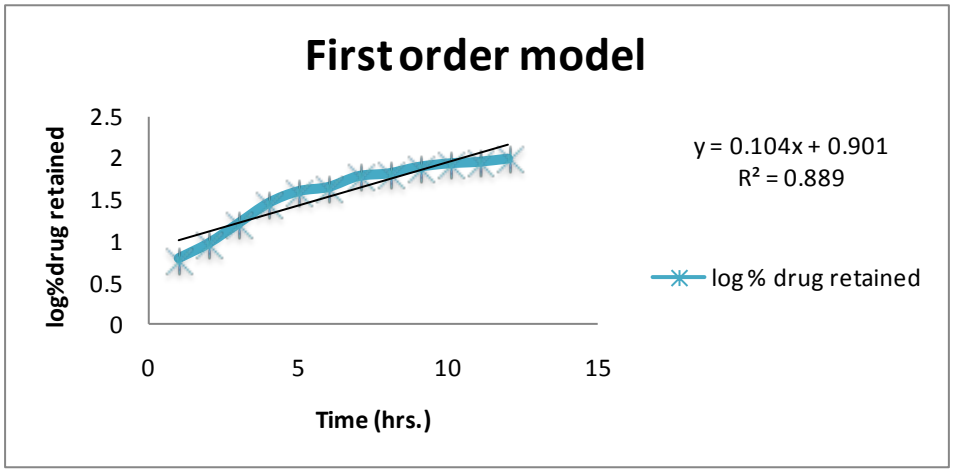


Figure iv: In vitro release profile of Oxcarbazepine for first order release kinetics for optimized formulation F9

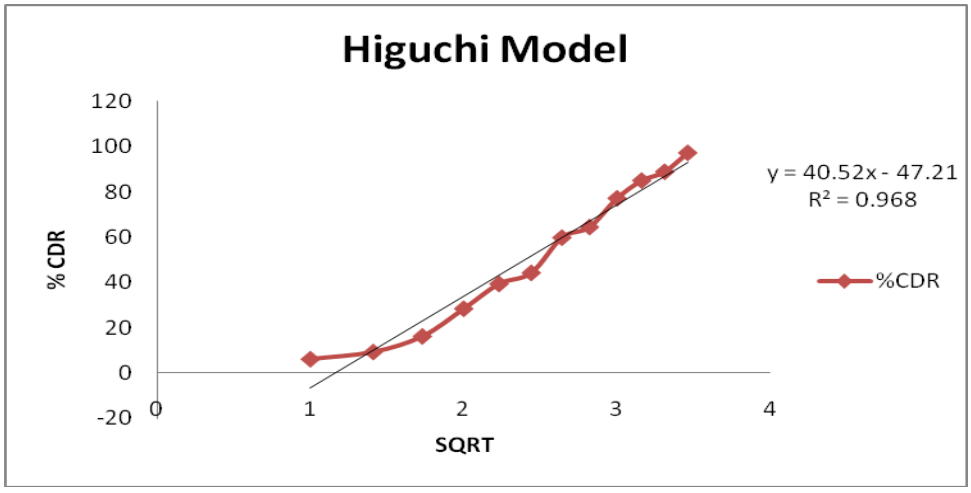


Figure v: In vitro release profile of Oxcarbazepine for higuchi model release kinetics for optimized formulation F9

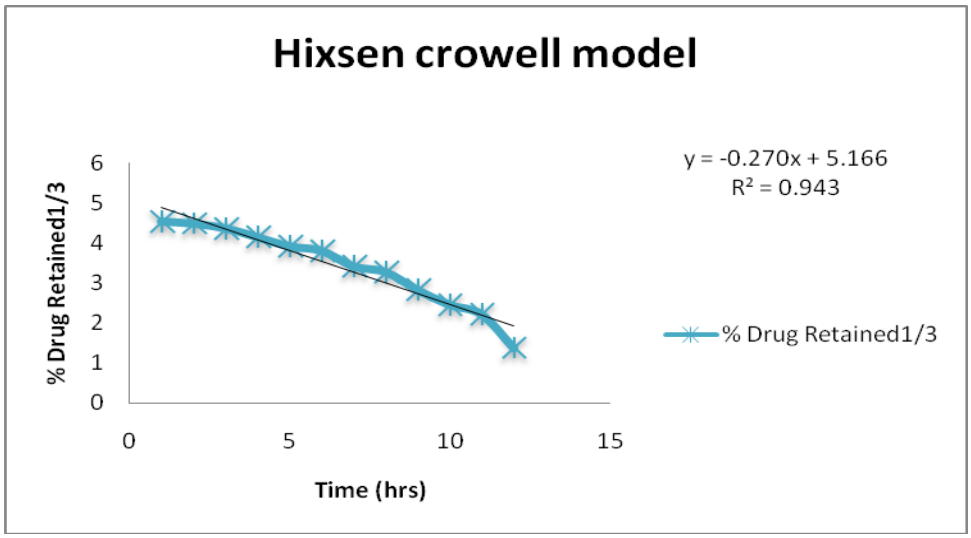


Figure vi: In vitro release profile of Oxcarbazepine for Hixsencrowell model release kinetics for optimized formulation F9

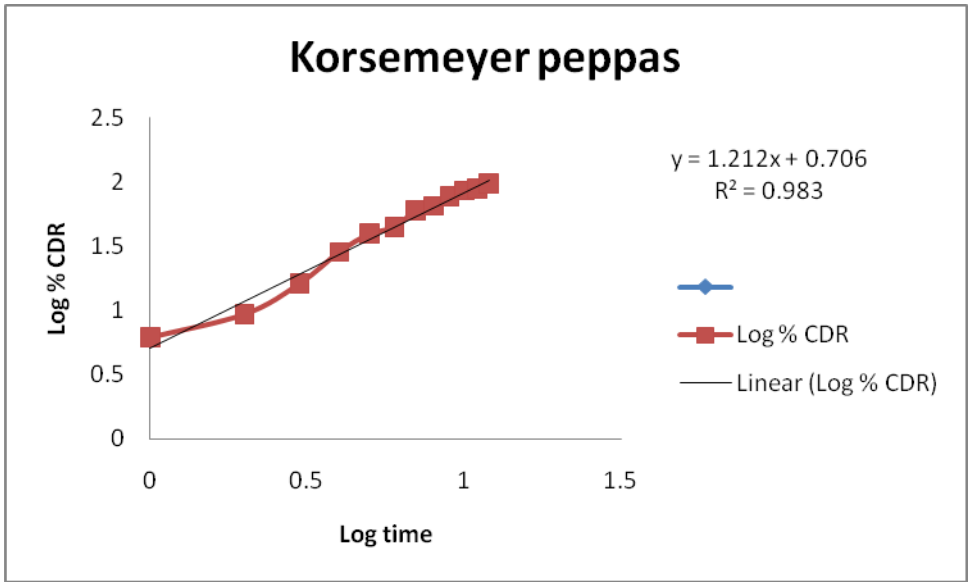


Figure vii: In vitro release profile of Oxcarbazepine for Korsemeyerpeppas release kinetics for optimized formulation F9

Table 13: In –vitro release profile of optimized formulation f9 for studying the release kinetics

Formulation F9	Zero order	First order	Higuchi	Hixsencrowell	Korsemeyerpeppas
	Y=8.8724×-6.2659 R^2=0.9917	Y=0.1049×+0.9015 R^2=0.8894	Y=40.529×-47.216 R^2=0.968	Y=-0.2709×+5.1665 R^2=0.9431	Y=1.2124×+0.7067 R^2=0.9838

Table 14:Result of microbiological test

Test	Result
Escherichia coli	Not Found
Salmonella	Not Found
Pseudomonas aeruginosa	Not Found
Staphylococcus aureus	Not Found

Stability Studies

Table 15: Stability Studies data of F9 Formulation during stability studies at $30^0 \pm 2^0$C and 60±5% RH

Parameter	Duration of 1 Month
Hardness(kg/cm^2)	7.99
Friability	0.3 56
Wt. variation (mg)	544.2
%Drug content	99.912

Table 16: In – vitro release profile of F9 during stability studies at $30^0 \pm 2^0$C and 60±5% RH for one month

Time (hrs.)	Cummulative % Drug release	
	Initial	After 1 Month
0	0	0
1	6.13	7.23
2	9.31	14.26
3	16.22	22.46
4	28.43	35.10
5	39.41	42.37
6	44.28	53.15
7	59.88	62.00
8	64.55	70.84
9	77.23	84.10
10	85.10	90.12
11	88.98	94.33
12	98.34	98.96

CONCLUSION

From the obtained results it can be concluded followings:-

- Oxcarbazepine is an antiepileptic drugs (AEDs).
- Melting point and IR indentification results of drugs indicates purity of drug.
- IR spectra of pure drug and excipients are indentical and from compatibility studies it was proved that there was no interaction between drug and excipients.
- Oxcarbazepine sustained release tablet was prepared by wet granulation technology.
- P.V.P.K. 30, H.P.M.C.K 100 M used as binder agent. And Cross Carmellose sodium used super disintegration agent.
- Colloidal silicone dioxide used tablet moisture adsorber and Glidant.
- Talcum used Glidant, and Magnesium Stearate used lubricant in tablet.

- Evaluation of pre compression parameter & post compression parameter were done and within the rang.
- The release rates of formulated tablets were performed up to 12 hrs.
- The microbial limit are within an acceptable range that does not pose diminished product stability.
- Comparable release profile of F9 after 1 month indicates stability of the formulation

ACKNOWLEDGMENT

First of all, I would like to express my salutation to GOD for giving me the strength, confidence and moral boost to successful completion of this project. It is with pleasure of immense gratitude that I express my most cordial and humble thanks to my esteemed teacher and guide **Mr. Anil Kumar Goyal**, Associate Professor , Department of Pharmaceutics , Mahatma Gandhi College of Pharmaceutical Sciences , Jaipur ,for his valuable guidance ,keen interest ,perennial inspiration and everlasting encouragement .I am gratefully indebted to **Mr. Amit Sharma**, Principal, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur, for providing necessary Facilities to carry out my work and for his constant support and encouragement.I would also like to thanks D.D. Pharmaceutical Pvt Ltd. Jaipur, specially **Mr. AmitChoudary** and **Mr. Prem Chand Satraval**. They had helpd me a lot during my disseratation work.

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