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FORMULATION AND EVALUATION OF CONTROLLED RELEASE MATRIX TABLETS OF PIRACETAM

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ABSTRACT

In present work attempts have been made to formulate controlled release matrix tablets of Piracetam by using natural & synthetic hydrophilic polymers, which is preferably used as ancognitive enhancer used in the treatment of Alzheimer's disease. Controlled release matrix tablets were prepared by using polymers such as HPMC (Hydroxy Propyl Methyl Cellulose) K-15M, Xanthan gum, SCMC (Sodium Carboxy Methyl Cellulose) in different concentration by wet granulation technique. Piracetam meets all the ideal characteristics to formulate as matrix type controlled release drug delivery system. Piracetam is a highly effective cognitive enhancer used as a model drug to develop a controlled release formulation. Piracetam exhibits pH dependent solubility. It is more soluble in acidic pH and slightly soluble at neutral or alkaline condition (intestinal environment). The λmax of Piracetam was found to be 201nm in 0.1N hydrochloric acid. The Piracetam obeys the Beer's law within the concentration of 5 to 25µg/ml. FTIR studies showed that there was no interaction between drug and polymers. The Controlled release matrix tablets were prepared by wet granulation method using different concentrations of gel forming natural & synthetic hydrophilic polymers. The formulated tablets were analyzed for pre compression and post compression parameter, swelling index, *in-vitro* drug release studies, *in-vitro* kinetics. The pre compression parameters of all the formulations were within the required limits was indicated good flow property, suitable for formulation of the tablets. The post compression parameters such as thickness, hardness, friability, uniformity of content and swelling index of all formulations were within the acceptable limits. F4 formulation was

selected as best formulation based on in-vitro release studies, swelling studies, in- vitro release kinetics. The extent of drug release was found to be 99.75 in 12hrs. The drug release model of this formulation (F4) complies with zero order kineticsfollowed by Non-fickian diffusion mechanism. FTIR of selected best formulation shows that no interaction between the drug and polymers. Selected formulation showed controlled release profile than the conventional tablet (F14).

KEYWORDS: Novel Drug Delivery, Controlled Release, Prolonged Action, Piracetam, Alzheimer's disease.

INTRODUCTION

In the last several decades, several types of dosage forms have been developed by scientists with certain patient favourable modifications, one of which is the oral drug delivery system which is the oldest one and has got popularity in for more than a century. Oral drug delivery system have the advantages that these are easy to administer, ease of manufacturing and higher patient compliance. In oral drug delivery systems certain modifications were done to achieve certain specific objectives, the most profound need of which was to maintain constant drug plasma concentrations for a certain period of time to reduce the dosage frequency which was achieved by controlled release drug delivery systems. The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. There is a continuously growing interest in the pharmaceutical industry for controlled release oral drug delivery systems. There is also a high interest for design a dosage formulation that allows high drug loading, particularly for actives with high water solubility. Controlled release systems provide a release profile independent of external environment and predominantly controlled by the design of the system. It implies a predictability and reproducibility in the drug release kinetics. That means, the release of drug ingredient(s) from a controlled-release drug delivery system proceeds at a rate profile that is predictable kinetically, and also reproducible from one unit to another **(Rani S.P et al., 2014).**

The plasma level of drug should be maintained within the safe margin and effective range, for this proper and calculated dose of the drug need to be given at different time intervals by conventional dosage forms **(Shalin A. Modi*et al*., 2011).**

Piracetam is an Cognitive enhancer widely used in the treatment of Alzheimer's disease, Dementia, Depression. Piracetam is chemically known as 2-(2-oxopyrrolidin-1-yl)acetamide. It is Freely soluble in water, methanol, DMSO and ethanol. Slightly soluble in methylene chloride. Piracetam is rapidly and extensively absorbed following oral administration. In fasted subjects, the peak plasma concentration are achieved 1hr after dosing. The absolute bioavailability of Piracetam oral formulations is close to100%. Food does not affect the extend of absorption of Piracetam. Piracetam is not bound to plasma protein and its volume of distribution is approximately 0.61/kg in animals Piracetam highest concentration in the brain were in the cerebral cortex and basal ganglia. Piracetam diffuses to all tissue except adipose tissue cross placental barrier and penetrates the membrane of isolated red blood cells. The plasma half-life of Piracetam in adults is about 5hrs following oral administration. The apparent total body clearance is 80-90ml/min. the major route of excreation is via urine, according for 80-100% of the dose. Piracetam is excreted by glomerular filtration.

MATERIALS AND EQUIPMENTS

S. No	Equipment's / Instruments	Manufacturer / Supplier
1	Electronic weighing balance	A & D company HR 200, Japan.
2	Hot air oven	RANDS Instruments Company, Chennai.
3	Single Punch tablet compression machine	CadmachMachinaryCo.Pvt., Ahmadabad
4	Vernier caliper	Linker, Mumbai.
5	Monsanto hardness tester	Praveen Enterprises, Bangalore.
6	Friability Test Apparatus	Indian Equipment Corporation.
7	pH meter	MC Dalal, Chennai
8	Digital Tablet Dissolution Test Apparatus	Disso 2000 Lab India, Mumbai.
9	UV-visible spectrophotometer	UV-1700 Pharmaspec Shimadzu, Japan
10	Fourier transform infra-red spectrophotometer	Shimadzu RXI Japan.

S. No	Name of material	Manufacturer / supplier	Use in formulation
1	Piracetam	Madras pharmaceutical pvt.Ltd.	Active ingredient
2	HPMC K15	Fourrts India Laboratories Pvt Ltd.	Hydrophilic polymer
3	Xanthan Gum	Fourrts India Laboratories Pvt Ltd.	Natural polymer
4	SCMC	Fourrts India Laboratories Pvt Ltd.	Hydrophilic polymer
5	Lactose	Fourrts India Laboratories Pvt Ltd.	Diluent
6	PVP K30	Fourrts India Laboratories Pvt Ltd.	Binder
7	Talc	Fourrts India Laboratories Pvt Ltd.	Glidant
8	Magnesium Stearate	Fourrts India Laboratories Pvt Ltd.	Lubricant

METHOD OF PREPARATION

The controlled release matrix tablets of Piracetam prepared using different polymers alone and in combination with varying ratios as summarized in (Table2) controlled release matrix tablets were prepared by wet granulation procedure involving two consecutive steps. The drug polymer mixture was prepared by homogeneously mixing the drug and polymers and other excipients in a glass mortar for 15min and polyvinyl pyrrolidone was added as a binding agent up to the formation of mass. These mass was passed through the 8mm screen mesh to form the granules. Then the formulated granules were dried in hot air oven at 60^{o}C for 15mins. Magnesium stearate was added as a lubricant in the granules and mixed. The blended granules were then compressed on tablet compression machine.

EVALUATION OF CONTROLLED MATRIX TABLETS PIRACETAM

Preparation of calibration curve

1. A. STANDARD CURVE FOR PIRACETAM

a). Preparation of dissolution medium

0.1N HCl

8.5ml of hydrochloric acid in 1000ml distilled water

b). Estimation of absorption maximum (λmax) for Piracetam by UV Spectroscopy

The standard stock solution of Piracetam having concentration 1000µg/ml is prepared by dissolving 100mg of Piracetam is diluted with 0.1N HCl up to 100ml. The stock solution is further diluted using 0.1N Hcl to produce 10µg/ml concentration. The resultant solution is scanned between wavelengths of 200-400 nm by UV Spectrophotometer. (UV-1700 Shimadzu Corporation, Japan) to get absorption maximum (λmax).

c). Preparation of standard calibration curve for Piracetam

From the above stock solution, aliquots are taken into different volumetric flasks and volume are made up to 100 ml with 0.1N HCl solution, so as to get concentration of 5, 10, 15, 20, 25 µg/ml. The absorbance of these solutions are measured at 201nm by UV Spectrophotometer. A calibration curve is plotted by taking concentration on X-axis and absorbance on Y-axis to obtain the standard curve. **(US Pharmacopoeia)**

1. B. STANDARD CURVE FOR PIRACETAM

a). Estimation of absorption maximum (λ max) for Piracetam by UV Spectroscopy

The standard stock solution of Piracetam having concentration 1000µg/ml is prepared by dissolving 100mg of Piracetam is diluted with distilled water up to 100ml. The stock solution is further diluted using distilled water to produce 10µg/ml concentration. The resultant solution is scanned between wavelengths of 200-400 nm by UV Spectrophotometer. (UV-1700 Shimadzu Corporation, Japan) to get absorption maximum (λmax).

b). Preparation of standard calibration curve for Piracetam

From the above stock solution, aliquots are taken into different volumetric flasks and volume are made up to 100 ml with distilled water solution, so as to get concentration of 5, 10, 15, 20, 25 µg/ml. The absorbance of these solutions are measured at 201 nm by UV Spectrophotometer. A calibration curve is plotted by taking concentration on X-axis and absorbance on Y-axis to obtain the standard curve. **(US Pharmacopoeia)**

1. C. STANDARD CURVE FOR PIRACETAM

a). Preparation of dissolution medium

Acid buffer PH 2.2: (Indian pharmacopoeia 1996, volume: 2, page no: A-144)

Place 50ml of 0.2M potassium chloride in a 200ml volumetric flask, add the Specified volume of 0.2M hydrochloric acid and then add water to volume.

Preparation of 0.2M potassium chloride

Dissolve 14.911gm of potassium chloride in water and dilute with water to 1000ml.

Preparation of 0.2M Hydrochloric acid

Hydrochloric acid diluted with water to contain 7.8ml of HCl in 1000ml.

b). Estimation of absorption maximum (λmax) for Piracetam by UV Spectroscopy

The standard stock solution of Piracetam having concentration 1000µg/ml is prepared by dissolving 100mg of Piracetam is diluted with Acidic buffer pH 2.2 up to 100ml. The stock solution is further diluted using acidic buffer pH 2.2 to produce 10µg/ml concentration. The resultant solution is scanned between wavelengths of 200-400 nm by UV Spectrophotometer. (UV-1700 Shimadzu Corporation, Japan) to get absorption maximum (λmax).

c). Preparation of standard calibration curve for Piracetam

From the above stock solution, aliquots are taken into different volumetric flasks and volume are made up to 100 ml with Acidic buffer pH 2.2 solution, so as to get concentration of 5, 10, 15, 20, 25µg/ml. The absorbance of these solutions are measured at 201 nm by UV Spectrophotometer. A calibration curve is plotted by taking concentration on X-axis and absorbance on Y-axis to obtain the standard curve. **(US Pharmacopoeia)**

2. DRUG-POLYMER COMPATIBILITY STUDIES

The compatibility studies are carried out by Infrared spectroscopy in order to evaluate the drug polymer interaction.

Fourier Transform Infrared Spectroscopic studies (FTIR)

Drug- polymer/excipients interactions play a vital role in the release of drug from formulation. Fourier transform infrared spectroscopy (FTIR) has been used to study the physical and chemical interactions between drug and the excipients used. The study is carried out by KBr pellet technique. Materials are compressed under 10 tones pressure in a hydraulic press to form a homogeneous sample/KBr pellet. The pellet is scanned over the frequency range from 4000 to 450 cm-1 and peaks obtained are identified.

Pre compressional evaluation of powder blend: (Dongre et al., 2015: AvaruGeethaDutt et al., 2014)

i). Angle of repose

The flow characteristics are evaluated by determining angle of repose. Improper Flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. Angle of repose is calculated using the equation.

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

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

Angle of repose	Type of flow
<20˚	Excellent
20˚-30˚	Good
30˚-35˚	Moderate
35˚-40˚	Poor
>40˚	Very poor

ii). Bulk Density

Apparent bulk density is determined by pouring pre sieved drug excipients blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/mL and is given by,

$$Db = M / VO$$

Where, Db is the bulk density, M is the mass of powder and VO is the Bulk volume of the powder.

iii). Tapped density

It is determined by placing a graduated cylinder, containing a known mass of drug excipients blend, on mechanical tapping apparatus. The tapped volume is measured by tapping the powder to constant volume. It is expressed in g/mL.

$$Dt = M / Vt$$

Where,

Dt is the tapped density,

M is the mass of powder and

Vt is the tapped volume of the powder.

iv). Compressibility index (or) Carr's Index (I)

Compressibility index is an important measure that can be obtained from the bulk and tapped densities. A material having values less than 20 to 30% is defined as the free flowing material, based on the apparent bulk density and tapped density. The percentage compressibility of the bulk drug is determined by using the following formula.

$$I = Dt – Db / Dt \times 100$$

Compressibility index (%)	Type of flow
10	Excellent
11-15	Good
15-20	Fair
21-25	Passable
26-31	Poor
32-37	very poor

v). Hausner's ratio

It indicates the flow properties of the powder. The ratio of Tapped density to bulk density of the powder or granules is called Hausner's ratio.

$$H = Dt / Db$$

Where,

H is the Hausner's ratio,

Dt is the tapped density of the powder and

Db is the bulk density of the powder.

Hausner's ratio	Type of flow
1-1.11	Excellent
1.12-1.18	Good
1.19-1.25	Fair
1.26-1.34	Passable
1.35-1.45	Poor
1.46-1.54	very poor
>1.60	very very poor

b). Post compressional evaluation of Piracetam controlled release matrix tablets (Dongre et al., 2015; Jaimini M, et al., 2007)

i). General appearance

The formulated tablets are evaluated for general appearance. Viz., color, odour, shape.

ii). Tablet Dimension

The thickness and diameter of the tablets are carried out using digital vernier caliper. Three tablets are used from each batch and results are expressed in millimeter (mm).

iii). Weight variation test

Twenty tablets are selected at random, individually weighed in a single pan electronic balance and the average weight is calculated. The uniformity of weight is determined according to I.P. specification. As per IP not more than two of individual weights should deviate from average weight by more than 5% and none deviate more than twice that percentage**.** The following percentage deviation in weight variation is shown in the table. **(IP.2007).**

Average weight of a tablet	Percentage deviation
Less than 80mg	±10%
More than 80mg to less than 250mg	±7.5%
250mg or more	±5%

iv). Hardness test

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing and shipping. Monsanto

hardness tester is used to measure the hardness of tablet. Three tablets from each batch are used for hardness test and results are expressed in Kg/cm^2.

v). Friability test

It is done in Roche friabilator apparatus where the tablets are subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm for dropping the tablets at a distance of six inches with each revolution. Pre weighed samples of 20 tablets are placed in the friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed. Compressed tablets that loss less than 0.5 to 1.0% of their weight are generally considered acceptable. The percentage friability is calculated by the following expression,

$$\text{Friability} = \frac{\text{Weight loss}}{\text{Weight of tablets before operations}} \times 100$$

vi).a) Drug content uniformity

Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 100mg of drug is taken in a 100ml volumetric flask and 0.1N HCl is added. The solution is filtered using membrane filter (0.45µm) and 10 ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with 0.1N HCl. Then 10ml of filtrate is taken from above solution and made up to final volume with 0.1N HCl. Then its absorbance is measured at 201nm using UV Visible spectrometer. The amount of drug present in one tablet is calculated using standard graph.

vi).b) Drug content uniformity

Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 100mg of drug is taken in a 100ml volumetric flask and distilled water is added. The solution is filtered using membrane filter (0.45µm) and 10 ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with distilled water. Then 10ml of filtrate is taken from above solution and made up to final volume with distilled water. Then its absorbance is measured at 201nm using UV Visible spectrometer. The amount of drug present in one tablet is calculated using standard graph.

vii).c) Drug content uniformity

Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 100mg of drug is taken in a 100ml volumetric flask and Acid buffer PH 2.2 is added. The solution is filtered using membrane filter (0.45µm) and 10

ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with Acid buffer PH 2.2. Then 10ml of filtrate is taken from above solution and made up to final volume with acid buffer pH 2.2. Then its absorbance is measured at 201nm using UV Visible spectrometer. The amount of drug present in one tablet is calculated using standard graph.

vii) Determination of Swelling Index: (Ravikumar et al., 2009)

Swelling of tablet excipients particles involves the absorption of a liquid resulting in an increasing in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecules. The liquid enters the particles through pores and bind to large molecule, breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of percentage weight gain by the tablet.

Method

For each formulation batch, one tablet was weighed and placed in a beaker containing 200 ml of buffer media. After each interval the tablet was removed from beaker and weighed again up to 8 hours. The swelling index was calculated using following formula.

$$\text{Swelling Index (\%)} = \frac{Wt - W0}{W0} \times 100$$

Where,

SI is swelling index,

Wt is weight of tablet at time t,

Wo is weight of tablet before immersion.

viii). In vitro drug release studies: (Karthik raja .M et al., 2012)

`Dissolution characteristics of the formulated controlled release matrix tablets of Piracetam are carried out using USP Type II (paddle) dissolution test apparatus for 12hrs.

Method

900 ml of dissolution medium was filled in dissolution vessel and temperature of the medium is set at 37°C ± 0.5°C. One tablet of different batch is placed in each dissolution vessel and the rotational speed of paddle was set at 50rpm. 4ml of sample is withdrawn at pre - determined time interval of every one hour for up to 12 hours and same volume of fresh medium is replaced immediately. The withdrawn sample is diluted to 25ml in volumetric

flask and filtered through 0.45µ membrane filter. 4ml of solution is withdrawn from above solutionand diluted to 25ml in volumetric flask. The resultant samples are analyzed for drug content at 201nm using UV-Visible spectrophotometer.

Parameter	Specifications
Dissolution Medium	Buffer 0.1N hydrochloric Acid, distilled water, acidic buffer pH2.2
Temperature	37.0 ± 0.5^{o}C
Initial Volume	900ml
Rotation Speed	50rpm
Drawn Volume	4ml
Running Time	12 hrs in 0.1N hydrochloric Acid, distilled water, acidic buffer pH2.2

ix). *Invitro* drug release kinetics (Reddy et. al., 2012)

To analyze the *In-vitro* release data various kinetic models were used to describe the release kinetics. The zero order rate describes the systems where the drug release rate is independent of its concentration. The first order describes the release from the system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on the Fickian diffusion. The Hixson-Crowell root law describes the release from the systems where there is a change in surface area and diameter of particles. The Koresmeyer-peppas describes the mode of release of drug from swellable matrices.

Release Kinetics Model	Equation
Zero Order	Qt = Q0 + K0.t
First Order	In Qt = In Q0 + K0.t
Hixson-Crowell	Q 01/3 – Qt 1/3 + K.t
Higuchi	Q = KH. t1/2
Koresmeyer – Peppas	Mt / M0 = a.tn

S. No.	Diffusion exponent value (n)	Drug release mechanism
1	< 0.5	Fickian release
2	0.5 to 1.00	non-Fickian transport
3	1.00	Case II transport
4	> 1.00	Super case II transport

The *in-vitro* release data are fitted to the above mathematical models and the applying data are,

- Cumulative % drug release vs. time for zero order kinetic.
- Log cumulative of % drug remaining vs. time for first order kinetic.
- Cumulative % drug release vs. Square root of time for Higuchi model.
- Log cumulative % drug release vs. log time for Korsmeyer-peppas model and

- Cube root of drug % remaining in matrix vs. time for Hixson-crowell cube root time.

x). Selection of best formulation

The best formulation is selected in accordance with the results obtained from swelling index, in-vitro drug release studies and kinetic analysis.

xi). Evaluation of selected best formulation

Infrared spectroscopic studies

The interaction between the drug and polymer are studied by FT-IR.

Comparison with conventional Formulation

The release of the best formulation is compared with the conventional formulation **(Pare A *et al*., 2008: Mahajan P *et al*., 2011).**

STABILITY STUDIES ON CONTROLLED RELEASE MATRIX TABLETS OF PIRACETAM

The purpose of stability testing is provides evidence on how the quality of an active substance or pharmaceutical product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light. In addition, product related factors such as the chemical and physical properties of the active substance and the pharmaceutical excipients, the dosage form and its composition, the manufacturing process, the nature of the container-closure system and the properties of the packaging materials, also influence the stability of the products. Another factor in stability is the possibility of the reaction or degradation products from excipients.

The stability of controlled release matrix tablets of piracetam in the present investigation was evaluated as per ICH guidelines.

In order to test the stability of the products, the storage conditions for accelerated testing (as per ICH and WHO) are $40^{o}C \pm 2^{o}C$ and 75% relative humidity (RH) ±5% for solid dosage forms for 6months. If the product is unstable in the above testing conditions, intermediate conditions, $30^{o}C \pm 2^{o}C$ and 80%RH±5% are recommended. WHO prescribed testing at 0, 1, 2, 3 and 6months during storage.

In the present study, as the formulation developed are solid dosage forms, a storage condition of $40^{o}C \pm 2^{o}C$, 75%±5% RH for 2months was used for accelerated testing. Controlled release

matrix tablet of piracetam formulation (F4) were tested for drug content, thickness, hardness, in-vitro release and swelling index at 0, 15, 30, 45 and 60days.

III. RESULTS AND DISCUSSION

Table 1: Calibration of Controlled Release Matrix Tablet of Piracetam.

S.NO:	CONCENTRATION	ABSORBANCE AT 201nm		
		0.1NHCl	Distilled water	Acidic buffer pH2.2
1.	5	0.236	0.212	0.175
2.	10	0.415	0.426	0.345
3.	15	0.603	0.625	0.504
4.	20	0.776	0.817	0.656
5.	25	0.981	0.991	0.837
REGRESSION VALUES		0.9996	0.9999	0.9996

Table 2: Formulation of Controlled Release Matrix Tablet.

S.no:	Ingredients	Quantity (mg) for one tablet (Average Weight-600mg)										
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
1	Piracetam	400	400	400	400	400	400	400	400	400	400	400
2	Xanthan gum	_	_	60	72	_	_	36	_	36	24	_
3	HPMC K15M	60	72	_	_	_	_	36	36	_	24	_
4	SCMC	_	_	_	_	60	72	_	36	36	24	_
5	MCC	116	104	116	104	116	104	104	104	104	104	176
6	PVP K 30	12	12	12	12	12	12	12	12	12	12	12
7	Isopropyl Alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
8	Magnesium stearate	6	6	6	6	6	6	6	6	6	6	6
9	Talc	6	6	6	6	6	6	6	6	6	6	6

Tables 3: Preformulations Study Of Controlled Release Matrix Tablets.

Batch Code	Angle of Repose	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Compressibility Index (%) +	Hausner's Ratio
F1	21°77'	0.4019±0.003	0.4356±0.004	7.72±0.9289	1.08±0.01
F2	22°45'	0.4064±0.003	0.4436±0.004	8.36±1.6054	1.09±0.02
F3	21°82'	0.4019±0.003	0.4436±0.004	9.37±1.8822	1.1±0.173
F4	21°78'	0.4064±0.003	0.4463±0.004	8.34±1.6475	1.09±0.02
F5	22°93'	0.4042±0.006	0.4463±0.004	9.41±2.4013	1.1±0.02
F6	22°93'	0.4019±0.003	0.4547±0.004	11.59±0.098	1.12±0.005
F7	23°26'	0.4111±0.006	0.4447±0.015	9.58±0.8500	1.10±0.011
F8	21°46'	0.3976±0.006	0.4412±0.013	9.79±1.7878	1.10±0.020
F9	22°29'	0.3891±0.007	0.4279±0.004	9.05±2.3101	1.11±0.01
F10	22°12'	0.3890±0.003	0.441±0.008	11.76±1.813	1.12±0.02
F11	22°61	0.4818±0.004	0.5124±0.006	5.97±0.08	1.06±0.001

Table 4: Post Compressional Evaluation of Controlled Release Matrix- Tablets.

Formulation code	Average weight	Diameter	Thickness	Hardness	Friability
F1	596.5±1.5	12	4.08±0.05	6.9±0.1	0.35±0.04
F2	596.5±1.3	12	4.04±0.05	6.7±0.1	0.33±0.08
F3	595.8±1.5	12	4.09±0.01	6.3±0.1	0.38±0.04
F4	597.5±1	12	4.1±0.01	7.4±0.1	0.41±0.08
F5	596.00±1	12	4.07±0.007	6.5±0.15	0.44±0.12
F6	598.2±1.07	12	4.08±0.008	6.8±0.15	0.33±0.08
F7	598.1±0.46	12	4.08±0.01	6.9±0.11	0.47±0.05
F8	597.3±0.2	12	4.07±0.008	6.9±0.11	0.41±0.05
F9	597.3±1.2	12	4.06±0.01	6.8±0.1	0.58±0.08
F10	597.1±0.5	12	4.06±0.01	6.9±0.1	0.55±0.12
F11	596.5±0.5	12	4.03±0.16	4.1±0.1	0.44±0.12

Tables 5: Drug Content and Swelling Index for Formulation Containing Piracetam Tablets.

Formulation Code	Drug content			swelling index		
	0.1N HCl	Distilled water	Acid buffer pH 2.2	0.1N HCl	distilled water	acid buffer pH2.2
F1	99.91±0.05	98.06±1.37	99.42±0.82	50.23±0.37	45.61±0.19	43.78±0.81
F2	99.3±1.13	98.18±0.16	99.27±0.20	51.41±0.71	48.32±0.74	45.31±0.13
F3	99.75±0.48	99.18±0.46	99.70±0.81	53.10±0.28	51.30±0.23	50.67±0.62
F4	99.91±0.72	99.75±0.33	99.73±0.60	60.98±0.42	57.37±0.44	53.89±0.31
F5	99.59±0.50	99.15±0.34	99.70±0.81	50.89±0.76	45.63±0.12	41.78±0.11
F6	99.43±0.13	99.15±0.16	98.98±0.20	52.12±0.40	45.65±0.61	46.37±0.43
F7	99.51±0.72	99.02±0.68	99.56±0.20	52.19±0.10	48.30±0.52	48.19±0.72
F8	99.81±0.60	99.39±0.16	99.42±0.41	51.88±0.12	51.23±0.89	48.93±0.19
F9	99.67±0.77	99.40±0.53	99.270±20	52.54±0.19	49.92±0.43	50.30±0.73
F10	99.59±0.13	99.27±0.33	99.27±0.20	53.8±0.29	53.45±0.29	51.47±0.17
F11	99.27±0.76	98.71±0.59	98.03±0.58	-	-	-

Table 6a: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using 0.1 N Hcl.

Time in hrs	Cumulative % drug release				
	F1	F2	F3	F4	F5
1	6.13±0.12	7.52±0.84	9.06±0.15	11.45±0.15	6.08±0.53
2	18.70±0.23	18.04±0.56	19.72±0.30	18.90±0.25	17.04±0.77
3	26.33±0.12	26.07±1.02	28.76±0.37	27.83±0.22	21.91±0.81
4	36.48±0.45	35.07±0.34	38.47±0.36	33.67±0.61	28.63±0.56
5	45.53±1.23	47.79±1.62	48.92±0.59	43.42±0.48	36.31±1.17
6	52.63±0.98	53.83±1.28	56.55±1.01	52.49±0.54	42.60±1.01
7	63.15±1.12	65.01±0.34	67.72±1.15	64.08±0.61	58.38±1.43
8	72.81±0.76	73.23±0.83	75.17±1.27	74.53±1.69	67.16±0.65
9	81.39±1.56	82.62±0.91	85.77±0.91	83.57±1.02	72.76±0.56
10	86.23±0.56	85.26±0.71	89.65±1.85	86.01±0.59	84.77±0.54
11	90.56±0.48	91.24±0.39	92.19±1.01	91.80±0.35	89.73±1.12
12	96.99±1.04	97.54±1.01	98.35±0.06	99.75±0.23	96.49±0.34

Table 6b: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using 0.1 N Hcl.

Time in hrs	Cumulative % drug release				
	F6	**F7**	**F8**	**F9**	**F10**
1	7.73±0.98	8.95±0.34	9.38±0.45	5.84±0.24	5.84±0.24
2	18.33±0.12	19.15±0.54	21.03±0.39	16.20±0.56	18.82±0.23
3	23.35±0.76	24.24±0.61	25.85±0.36	24.68±0.67	24.68±0.15
4	30.38±1.32	33.48±0.97	35.50±0.13	35.18±0.39	35.18±0.32
5	40.57±0.12	45.52±1.47	46.42±1.03	45.37±0.02	45.37±0.09
6	50.22±0.13	53.25±1.45	53.62±1.15	53.10±0.35	53.10±0.35
7	60.14±1.78	59.14±1.57	60.90±0.53	63.32±0.29	63.32±0.29
8	68.17±0.23	69.74±1.29	71.69±0.94	75.32±0.42	75.32±0.35
9	77.33±1.34	79.05±1.70	82.84±0.54	82.17±0.18	82.17±0.19
10	86.14±1.21	87.41±0.57	89.46±0.90	87.14±0.17	87.14±0.14
11	91.02±1.68	92.49±1.19	92.88±0.61	91.09±0.42	91.09±0.54
12	97.39±0.28	98.07±0.63	98.36±0.39	98.03±0.05	99.03±0.05

Table 6c: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using Distilled Water.

Time in hrs	Cumulative % drug release				
	F1	F2	F3	F4	F5
1	6.08±0.54	5.82±0.45	8.95±0.36	9.38±0.49	5.75±1.36
2	17.04±0.87	17.31±0.89	19.15±0.84	21.03±0.49	16.86±1.03
3	21.91±0.87	27.99±0.45	24.24±0.71	25.85±0.36	27.14±0.31
4	28.63±0.76	35.10±0.37	33.48±0.65	35.50±0.93	34.83±0.99
5	36.31±1.45	42.04±0.56	45.52±1.34	46.42±1.53	42.68±0.67
6	42.60±0.23	49.45±0.37	53.25±1.89	53.62±1.55	51.07±0.57
7	58.38±1.34	54.64±0.72	59.14±1.09	60.90±0.76	61.81±1.25
8	67.16±0.85	60.73±0.56	69.74±1.56	71.69±0.54	76.08±.37
9	72.76±0.55	72.92±1.34	79.05±1.45	82.84±0.87	83.53±1.65
10	84.77±0.45	84.59±1.05	87.41±0.32	89.46±0.52	87.80±1.32
11	89.73±1.98	90.90±1.03	92.49±1.69	92.88±0.21	91.79±1.83
12	96.49±0.67	95.26±0.34	98.07±0.56	98.36±0.58	95.62±0.96

Table 6d: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using Distilled Water.

Time in hrs	Cumulative % drug release				
	F6	**F7**	**F8**	**F9**	**F10**
1	6.64±0.17	5.75±1.36	6.37±0.34	5.49±0.17	7.73±0.67
2	17.92±1.05	16.86±1.03	17.28±0.67	16.37±0.45	18.33±0.46
3	27.13±1.42	27.14±0.31	27.22±0.92	26.29±0.45	23.35±0.96
4	40.97±0.27	34.83±0.99	36.70±1.75	32.52±0.67	30.38±1.37
5	45.03±0.82	42.68±0.67	42.94±0.98	37.13±1.33	40.57±0.67
6	52.53±1.05	51.07±0.57	52.14±0.43	43.68±0.34	50.22±0.67
7	63.36±0.99	61.81±1.25	61.34±1.13	48.74±0.89	60.14±1.34
8	75.09±0.12	72.12±.37	70.12±0.53	53.13±0.45	68.17±0.78

9	84.19±0.77	83.53±1.65	80.12±0.58	57.72±0.87	77.33±1.34
10	90.04±0.94	87.80±1.32	86.26±0.31	62.05±1.12	86.14±1.27
11	92.25±0.73	91.79±1.83	90.12±0.53	73.55±1.21	91.02±1.69
12	96.08±0.27	95.62±0.96	93.52±0.59	90.35±0.34	97.39±0.25

Table 6e: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using Acid Buffer pH 2.2.

Time in hrs	Cumulative % drug release				
	F1	F2	F3	F4	F5
1	6.37±0.34	6.08±0.54	7.52±0.47	7.73±0.67	5.49±0.17
2	17.28±0.67	17.04±0.87	18.04±0.43	18.33±0.46	16.37±0.45
3	27.22±0.92	21.91±0.87	26.07±0.73	23.35±0.96	26.29±0.45
4	36.70±1.75	28.63±0.76	35.07±0.65	30.38±1.37	32.52±0.67
5	42.94±0.98	36.31±1.45	47.43±0.57	40.57±0.67	37.13±1.33
6	52.14±0.43	42.60±0.23	53.83±1.12	50.22±0.67	43.68±0.34
7	62.17±1.13	58.38±1.34	64.10±0.85	60.14±1.34	48.74±0.89
8	73.27±0.53	67.16±0.85	73.23±1.05	68.17±0.78	53.13±0.45
9	81.77±0.58	72.76±0.55	82.62±0.96	77.33±1.34	59.90±0.87
10	86.26±0.31	84.77±0.45	85.26±0.67	86.14±1.27	65.89±1.12
11	90.12±0.53	89.73±1.98	91.24±0.77	91.02±1.69	73.55±1.21
12	93.52±0.59	96.49±0.67	97.14±0.31	97.39±0.25	90.35±0.34

Table 6f: Invitro Drug Release Profile of Controlled Release Matrix Tablet of Piracetam Using Acid Buffer pH 2.2.

Time in hrs	Cumulative % drug release				
	F6	F7	F8	F9	F10
1	5.82±0.45	6.64±0.17	5.75±1.36	6.15±0.32	6.10±0.72
2	17.31±0.89	17.92±1.05	16.86±1.03	17.44±0.07	18.10±0.76
3	27.99±0.45	27.13±1.42	27.14±0.31	27.05±1.11	26.44±0.73
4	35.10±0.37	40.97±0.27	34.83±0.99	34.87±1.41	36.52±0.42
5	42.04±0.56	45.03±0.82	42.68±0.67	43.46±0.77	45.49±0.27
6	49.45±0.37	52.53±1.05	51.07±0.57	52.81±0.21	52.65±0.51
7	54.64±0.72	63.36±0.99	61.81±1.25	64.10±0.63	63.12±0.59
8	60.73±0.56	75.09±0.12	76.08±.37	75.71±0.42	72.76±0.85
9	72.92±1.34	84.19±0.77	83.53±1.65	82.65±0.81	81.32±0.50
10	84.59±1.05	90.04±0.94	87.80±1.32	88.01±0.33	86.02±0.15
11	90.90±1.03	92.25±0.73	91.79±1.83	92.08±1.27	90.19±0.35
12	95.26±0.34	96.08±0.27	95.62±0.96	94.48±0.34	96.97±0.23

Table 7a In-Vitro Release Kinetics Data Of Piracetam Controlled Release Matrix Tablets Using 0.1 N Hcl.

Formulation Code	Zero order		First order		Higuchi		Koresmeyer peppas		Hixson Crowell		Release Mechanism
	r^2	$K^0(h^{-1})$	r^2	K_1 (h^{-1})	r^2	K_H $(h^{-1/2})$	r^2	n	r^2	$K_{HC}(h^{-1/3})$	Non-fickian
F1	0.991	8.404	0.893	-0.117	0.938	31.63	0.984	0.969	0.970	-0.265	Non-fickian
F2	0.990	8.439	0.878	-0.121	0.938	31.79	0.993	0.926	0.966	-0.270	Non-fickian
F3	0.986	8.509	0.827	-0.102	0.946	32.24	0.995	0.967	0.926	-0.306	Non-fickian
F4	0.997	8.439	0.875	-0.123	0.951	31.64	0.997	0.911	0.966	-0.314	Non-fickian
F5	0.996	8.350	0.854	-0.111	0.900	30.76	0.991	0.989	0.938	-0.259	Non-fickian
F6	0.996	8.401	0.853	-0.119	0.915	32.01	0.995	0.949	0.918	-0.263	Non-fickian
F7	0.993	8.205	0.881	-0.115	0.929	31.41	0.996	0.974	0.868	-0.320	Non-fickian
F8	0.991	8.457	0.848	-0.133	0.934	31.74	0.995	0.949	0.950	-0.362	Non-fickian
F9	0.990	8.620	0.865	-0.127	0.930	32.33	0.989	0.918	0.963	-0.279	Non-fickian
F10	0.991	8.596	0.805	-0.137	0.931	32.25	0.984	0.996	0.941	-0.288	Non-fickian

Table 7b: In-Vitro Release Kinetics Data of Piracetam Controlled Release Matrix Tablets Using Distilled Water.

Formulation Code	Zero order		First order		Higuchi		Koresmeyer peppas		Hixson Crowell		Release Mechanism
	r^2	$K^0(h^{-1})$	r^2	K_1 (h^{-1})	r^2	K_H $(h^{-1/2})$	r^2	n	r^2	$K_{HC}(h^{-1/3})$	Non-fickian
F1	0.993	8.350	0.854	-0.111	0.900	30.76	0.991	0.822	0.938	-0.259	Non-fickian
F2	0.994	8.048	0.867	-0.105	0.924	30.03	0.982	0.864	0.938	-0.246	Non-fickian
F3	0.996	8.405	0.840	-0.127	0.929	31.41	0.996	0.957	0.944	-0.276	Non-fickian
F4	0.996	8.457	0.848	-0.133	0.937	32.10	0.995	0.820	0.984	-0.284	Non-fickian
F5	0.987	8.563	0.934	-0.116	0.934	31.74	0.985	0.847	0.977	-0.269	Non-fickian
F6	0.985	8.520	0.931	-0.120	0.936	32.14	0.985	0.901	0.977	-0.272	Non-fickian
F7	0.990	8.519	0.804	-0.139	0.928	31.92	0.986	0.848	0.884	-0.316	Non-fickian
F8	0.991	8.240	0.945	-0.103	0.937	31.01	0.988	0.883	0.982	-0.247	Non-fickian
F9	0.976	8.764	0.790	-0.065	0.917	24.97	0.970	0.854	0.878	-0.172	Non-fickian
F10	0.996	8.401	0.853	-0.119	0.919	31.21	0.995	0.903	0.946	-0.268	Non-fickian

Table 7c: In-Vitro Release Kinetics Data of Piracetam Controlled Release Matrix Tablets Using Acid Buffer pH 2.2

Formulation Code	Zero order		First order		Higuchi		Koresmeyer peppas		Hixson Crowell		Release Mechanism
	r^2	$K^0(h^1)$	r^2	K_1 (h^1)	r^2	K_H $(h^{-1/2})$	r^2	n	r^2	K_{HC} $(h^{-1/3})$	
F1	0.987	8.306	0.953	-0.104	0.936	31.29	0.987	0.882	0.984	-0.249	Non-fickian
F2	0.993	8.3505	0.854	-0.111	0.900	30.76	0.991	0.822	0.938	-0.259	Non-fickian
F3	0.990	8.422	0.892	-0.119	0.938	31.72	0.993	0.922	0.970	-0.267	Non-fickian
F4	0.996	8.773	0.853	-0.119	0.940	32.01	0.995	0.821	0.986	-0.268	Non-fickian
F5	0.983	8.048	0.812	-0.067	0.921	30.40	0.973	0.851	0.898	-0.176	Non-fickian
F6	0.994	8.401	0.867	-0.105	0.924	30.03	0.982	0.864	0.909	-0.241	Non-fickian

F7	0.985	8.520	0.886	-0.130	0.936	32.14	0.985	0.901	0.896	-0.319	Non-fickian
F8	0.987	8.563	0.934	-0.116	0.927	32.10	0.985	0.847	0.977	-0.269	Non-fickian
F9	0.986	8.505	0.949	-0.112	0.931	31.98	0.987	0.869	0.981	-0.264	Non-fickian
F10	0.991	8.403	0.892	-0.116	0.938	31.61	0.985	0.876	0.970	-0.264	Non-fickian

Table 7c: In-Vitro Release Kinetics Data of Piracetam Controlled Release Matrix Tablets Using Acid Buffer Ph 2.2.

Formulation Code	Zero order		First order		Higuchi		Koresmeyer peppas		Hixson Crowell		Release Mechanism
	r^2	$K^0(h^1)$	r^2	K_1 (h^1)	r^2	K_H $(h^{-1/2})$	r^2	n	r^2	K_{HC} $(h^{-1/3})$	
F1	0.987	8.306	0.953	-0.104	0.936	31.29	0.987	0.882	0.984	-0.249	Non-fickian
F2	0.993	8.3505	0.854	-0.111	0.900	30.76	0.991	0.822	0.938	-0.259	Non-fickian
F3	0.990	8.422	0.892	-0.119	0.938	31.72	0.993	0.922	0.970	-0.267	Non-fickian
F4	0.996	8.773	0.853	-0.119	0.940	32.01	0.995	0.821	0.986	-0.268	Non-fickian
F5	0.983	8.048	0.812	-0.067	0.921	30.40	0.973	0.851	0.898	-0.176	Non-fickian
F6	0.994	8.401	0.867	-0.105	0.924	30.03	0.982	0.864	0.909	-0.241	Non-fickian
F7	0.985	8.520	0.886	-0.130	0.936	32.14	0.985	0.901	0.896	-0.319	Non-fickian
F8	0.987	8.563	0.934	-0.116	0.927	32.10	0.985	0.847	0.977	-0.269	Non-fickian
F9	0.986	8.505	0.949	-0.112	0.931	31.98	0.987	0.869	0.981	-0.264	Non-fickian
F10	0.991	8.403	0.892	-0.116	0.938	31.61	0.985	0.876	0.970	-0.264	Non-fickian

Table 8: Evaluation of Piracetam Controlled Release Tablets Kept in Stability At 40^{o}C /75% Relative Humidity.

Formulation Parameters	Initial	15 days	30days	45days	60days
Average weight (mg)	597.5±1.5	597.3±1.07	597.0±1.1	596.96±1.0	596.91±1.01
Thickness (mg)	4.1±0.01	4.1±0.007	4.0±0.05	3.98±0.01	3.98±0.04
Hardness (kg/cm^2)	7.4±0.1	7.2±0.15	7.2±0.1	7.0±0.11	7.0±0.11
Drug content (%)	99.91±0.72	99.89±0.16	99.57±0.13	99.29±0.27	98.98±0.20
Swelling Index (8 Hours) (%)	60.98±0.42	60.95±0.37	60.90±0.58	60.88±0.76	60.88±0.51
cumulative % drug release	99.75±0.23	98.56±0.17	99.12±0.36	98.49±1.04	98.63±0.73

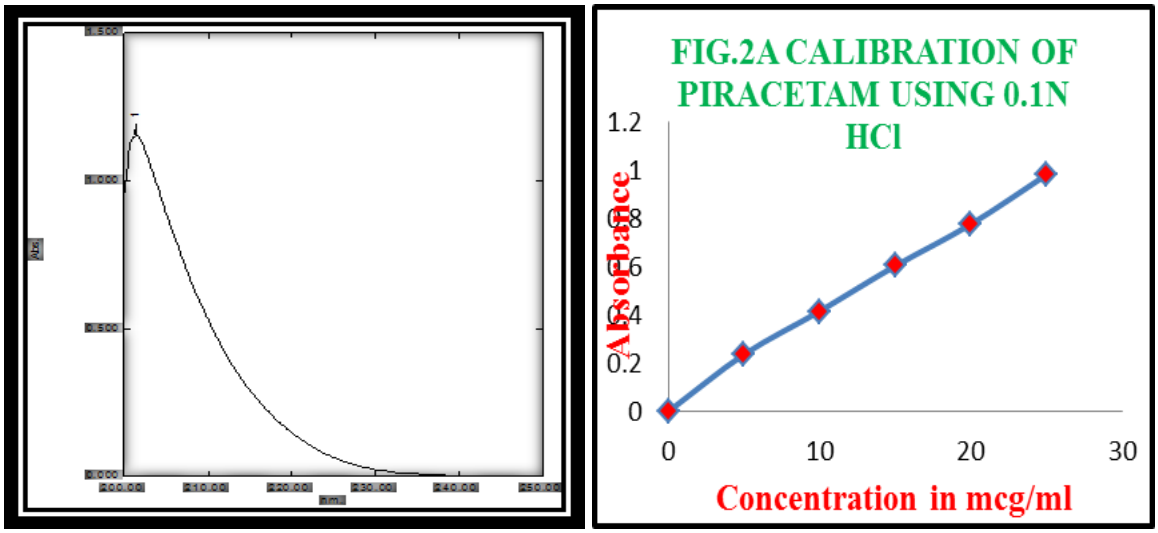
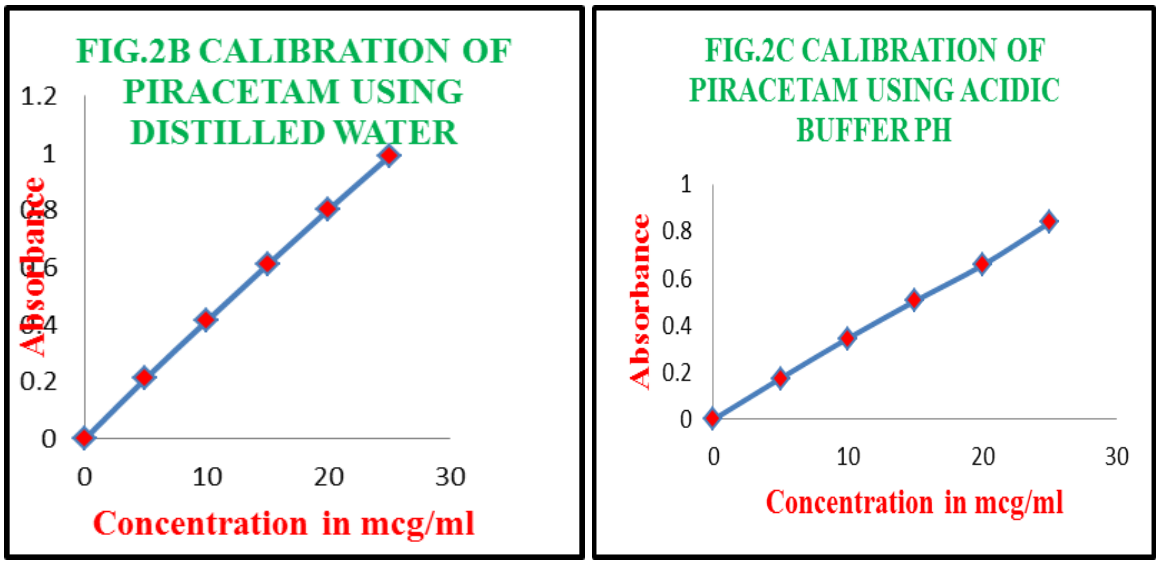


FIG.1: Determination of λmax of Piracetam.



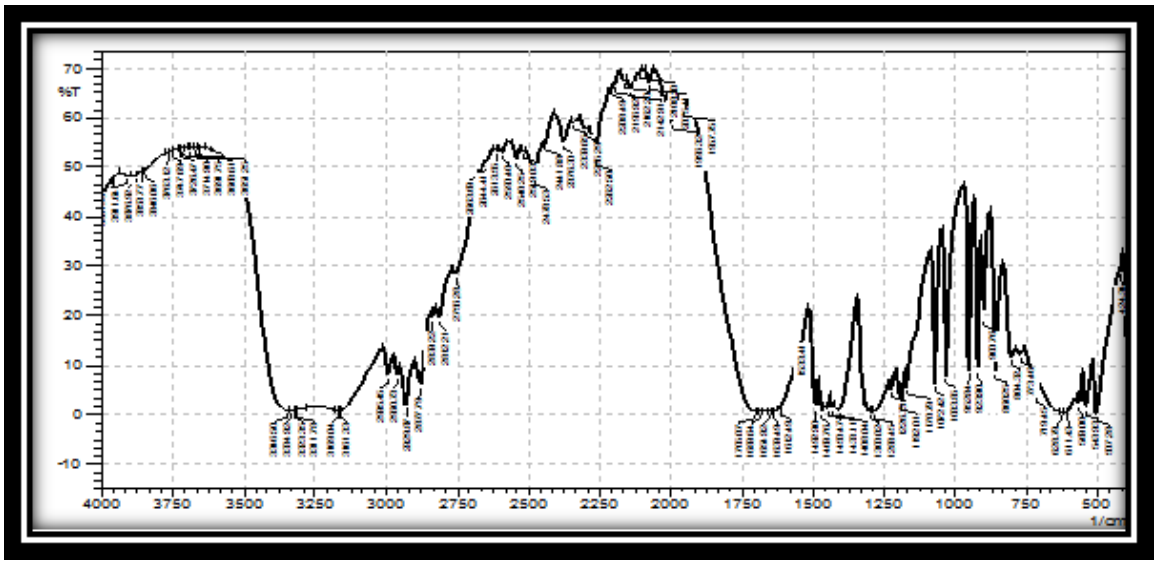


FIG.3A: FTIR Study of Piracetam Drug.

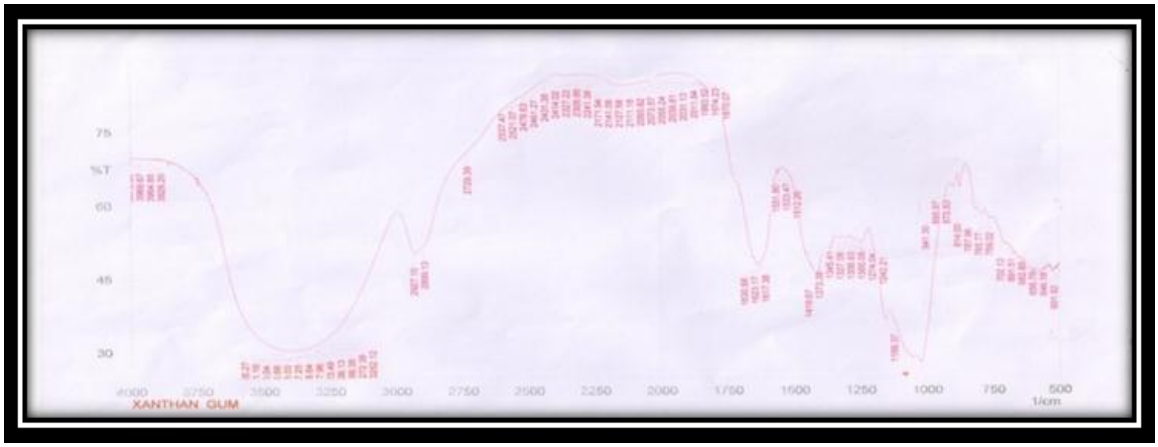


FIG.3B: FTIR Study of Xanthan Gum.

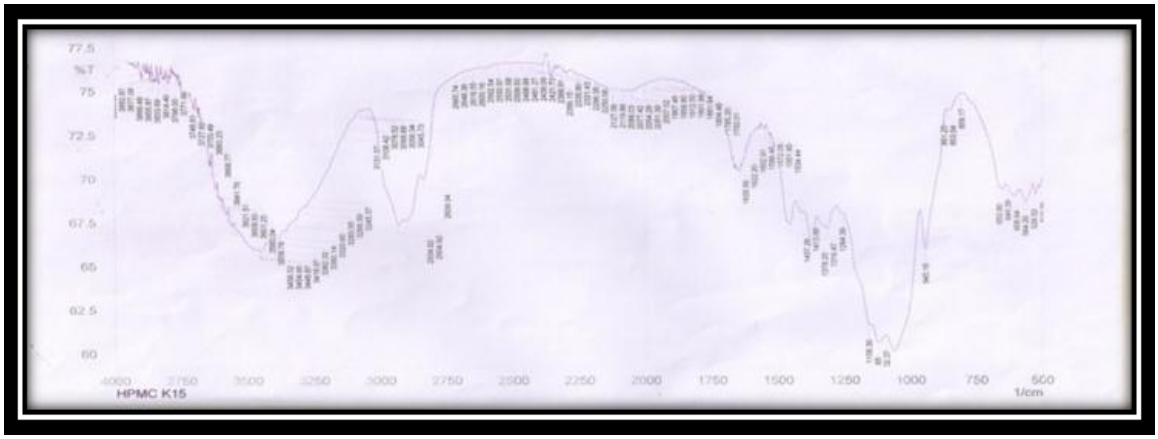


FIG.3C: FTIR Study of HPMC K15M.

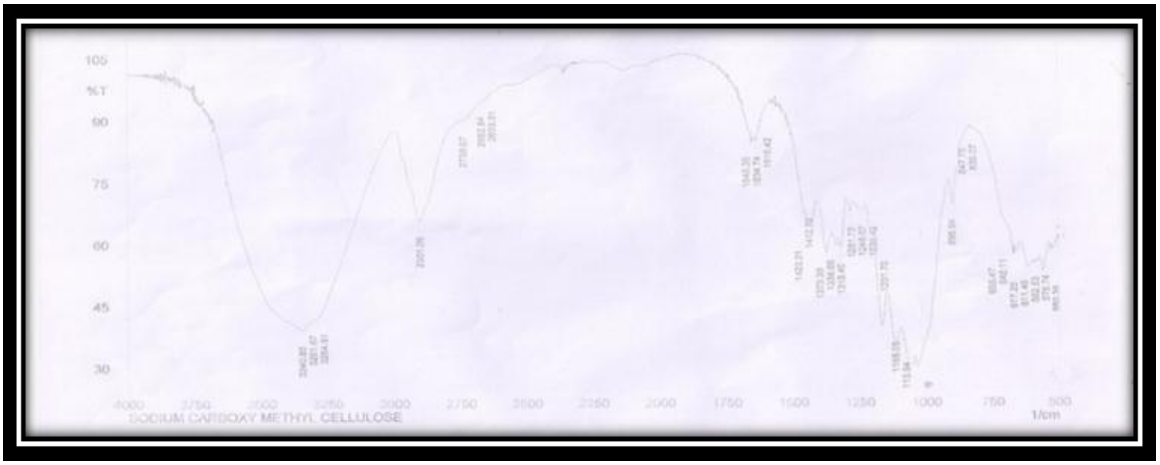


FIG.3D: FTIR Study of Sodium Carboxy Methyl Cellulose.

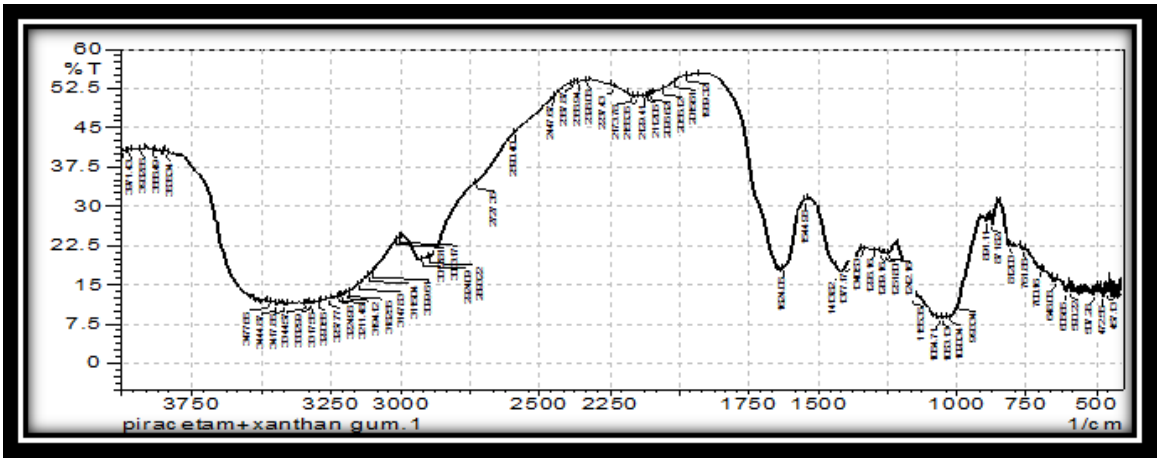


FIG.3E: FTIR Study of Piracetam+Xanthan Gum.

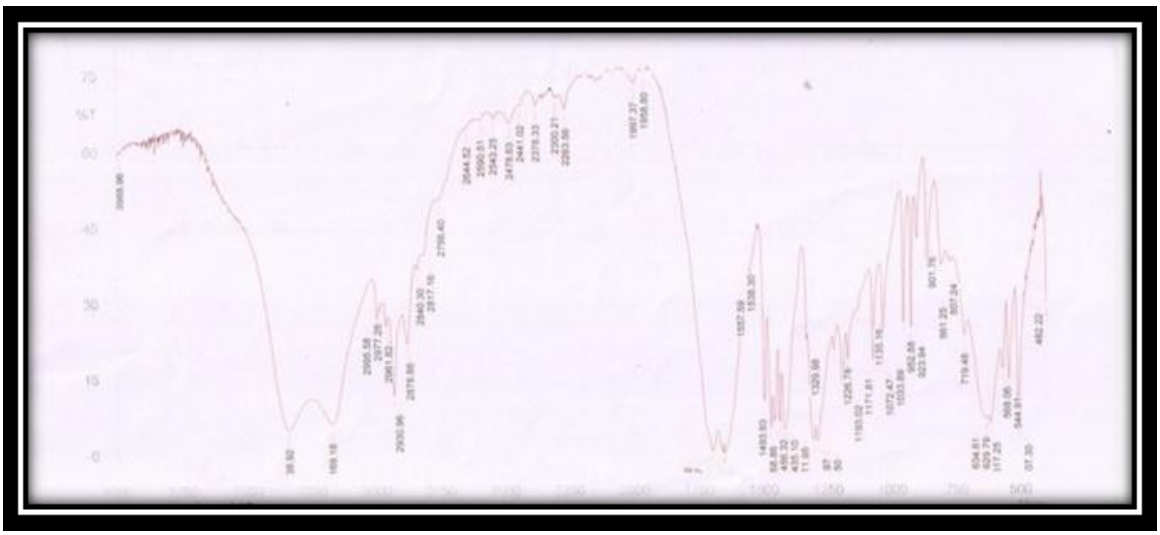


FIG.3F: FTIR Study of Piracetam+HPMC K15.

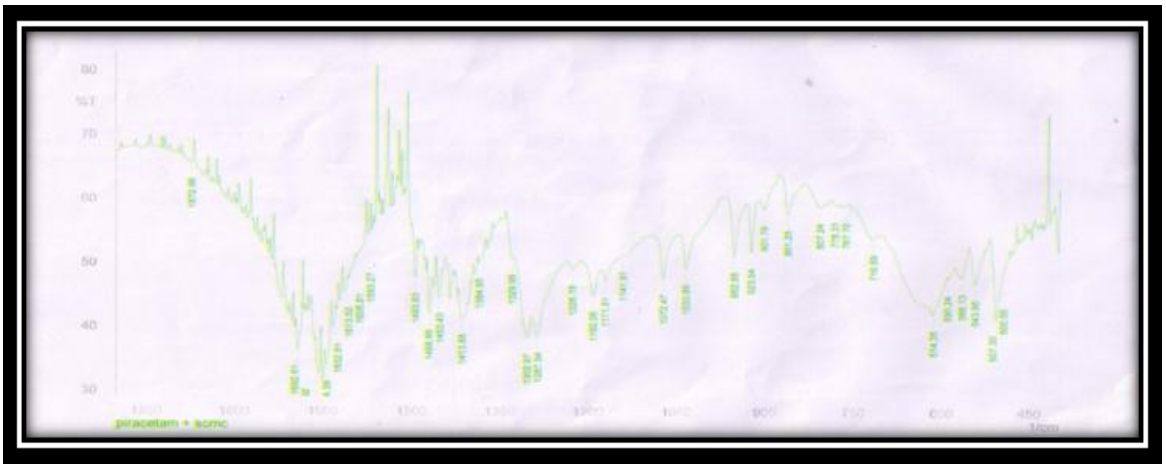


FIG.3G: FTIR Study of Piracetam+Sodium Carboxy Methyl Cellulose.

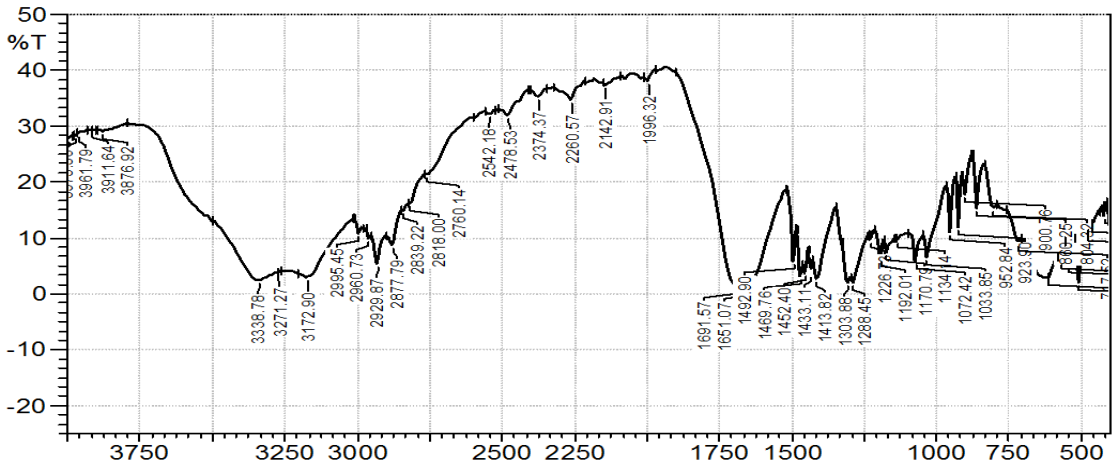


FIG.3H: FTIR Study of Piracetam+Xanthan Gum+HPMC K15+SCMC.

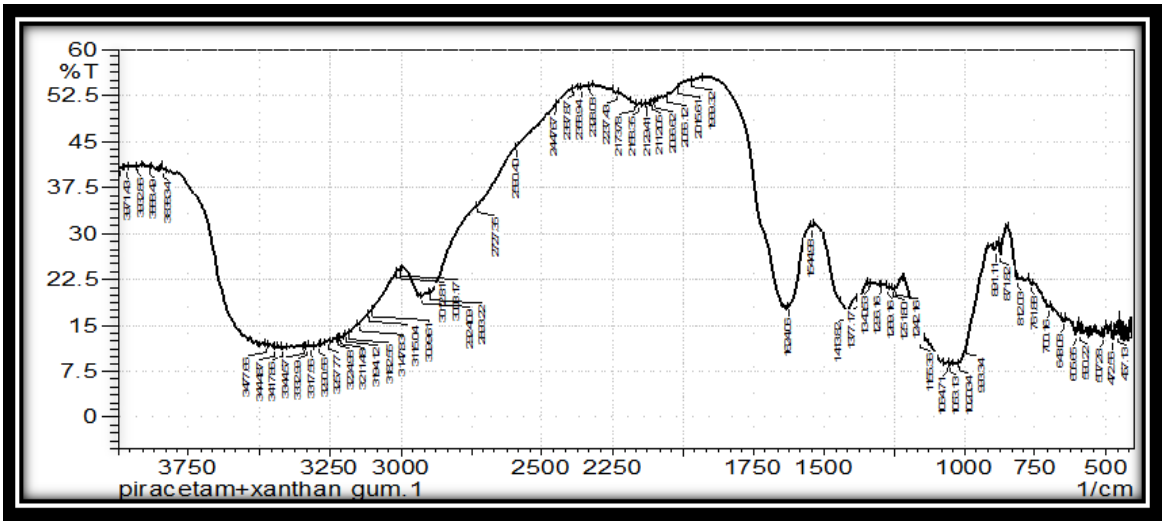


FIG.4: FTIR Study of Best Formulation (F4).

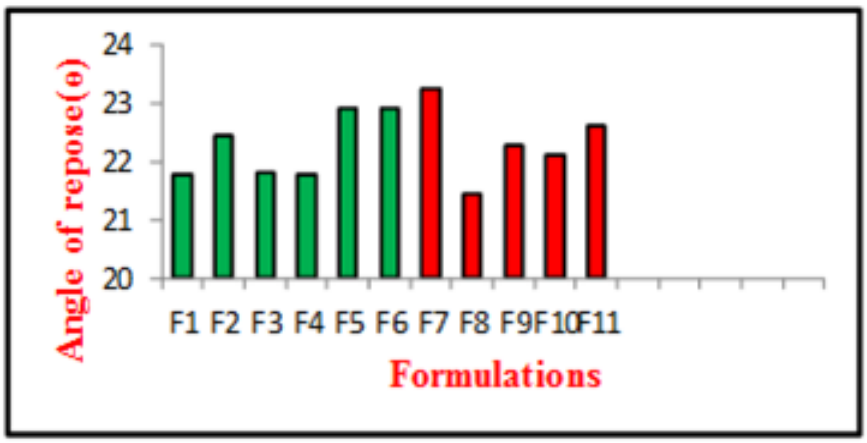


Fig. 5: Angle of Repose of All Formulations (F1-F11).

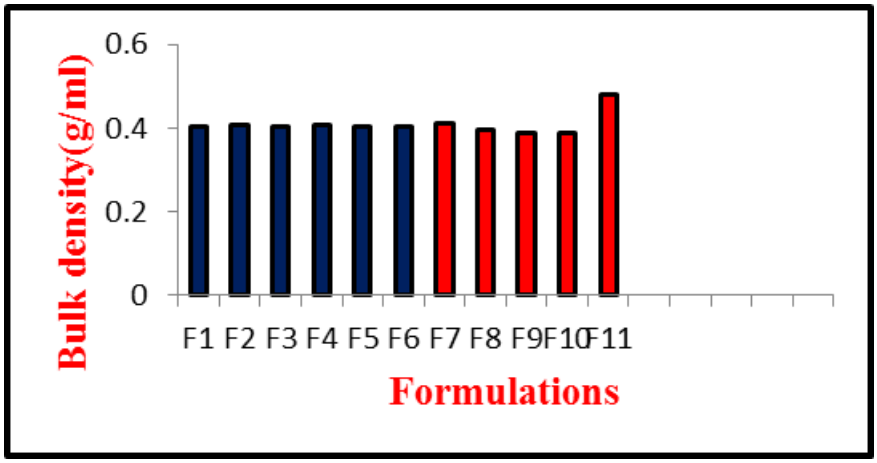


FIG.6: Bulk Density of All Formulations (F1-F11).

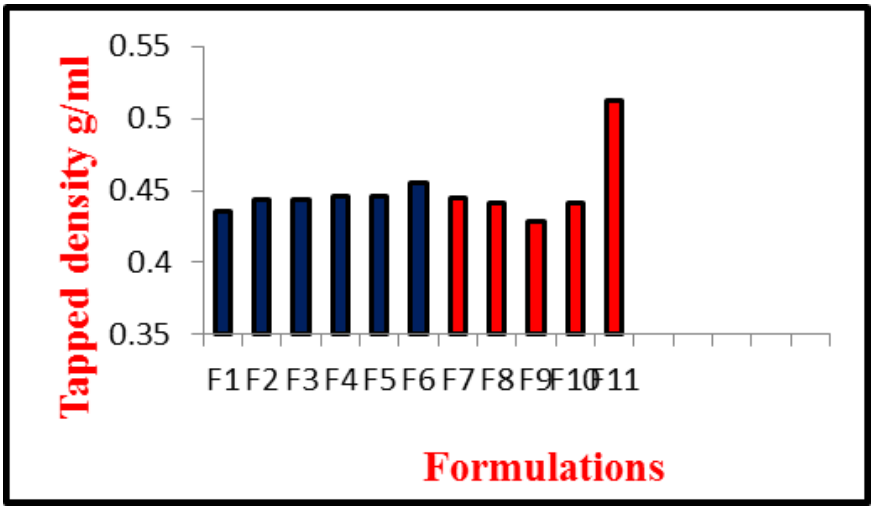


FIG.7: Tapped Density of All Formulations (F1-F11).

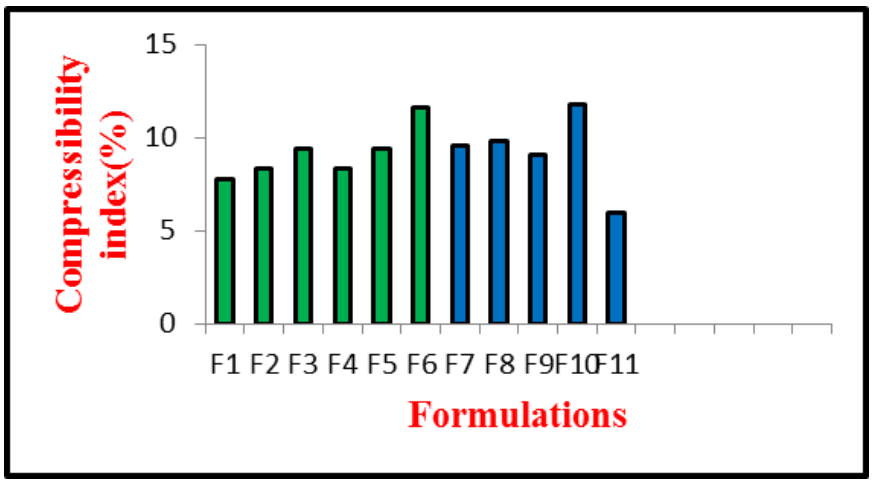


FIG.8: Compressibility Index of All Formulations (F1-F11).

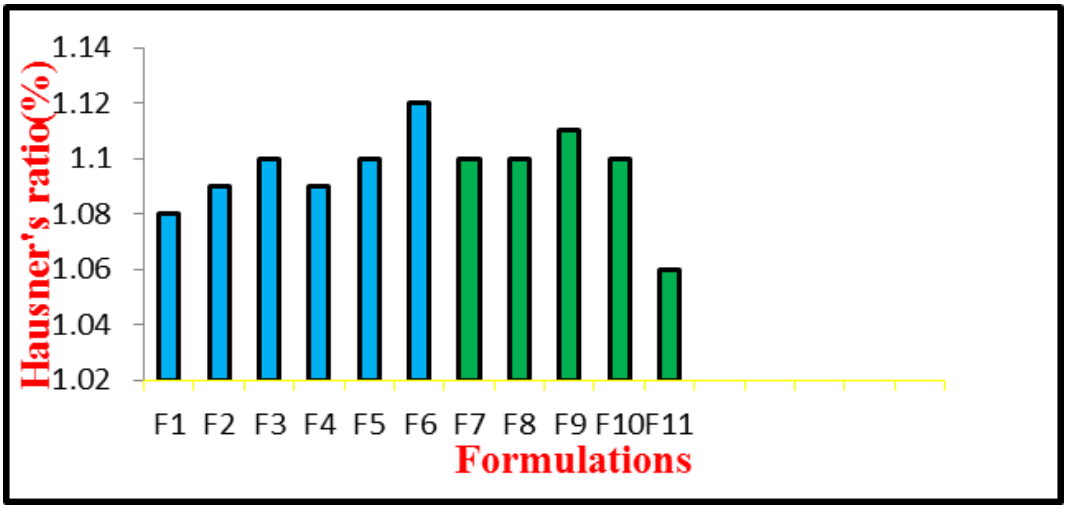


FIG.9: Haushner Ratio of Formulations (F1-F11).

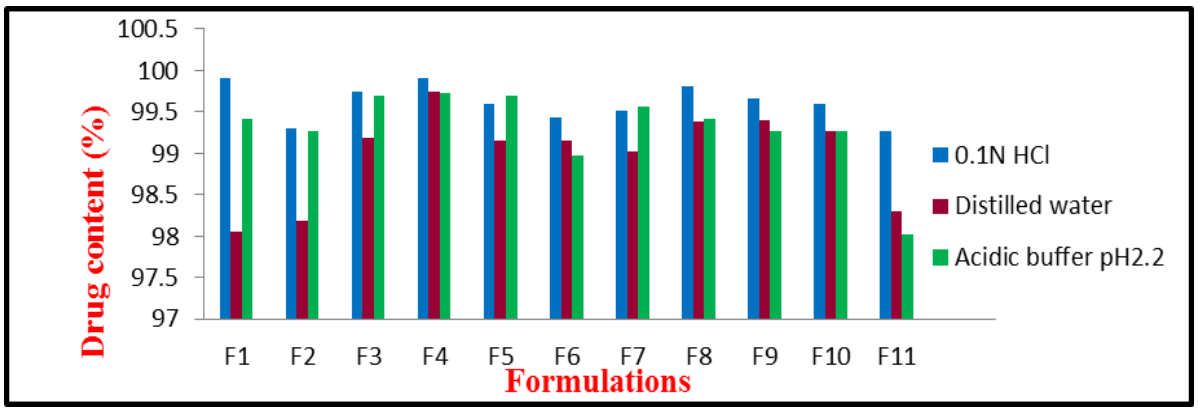


FIG.10: Drug Content of All Fomulations (F1-F11) Using 0.1N Hcl, Distilled Water and Acidic Buffer pH 2.2.

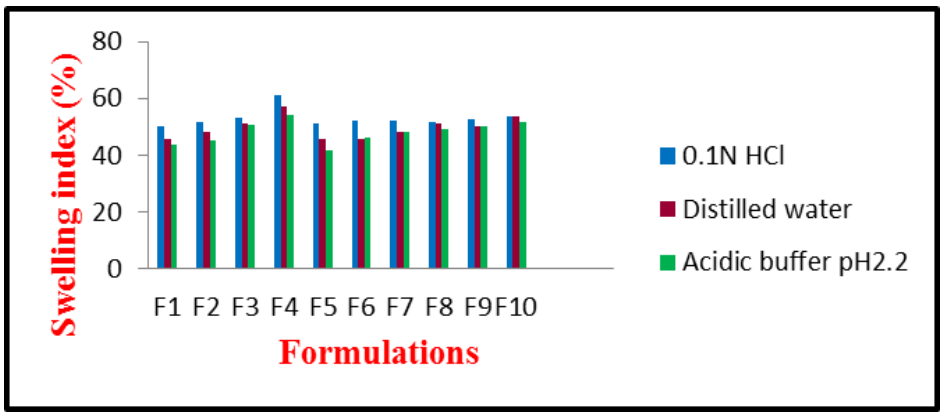
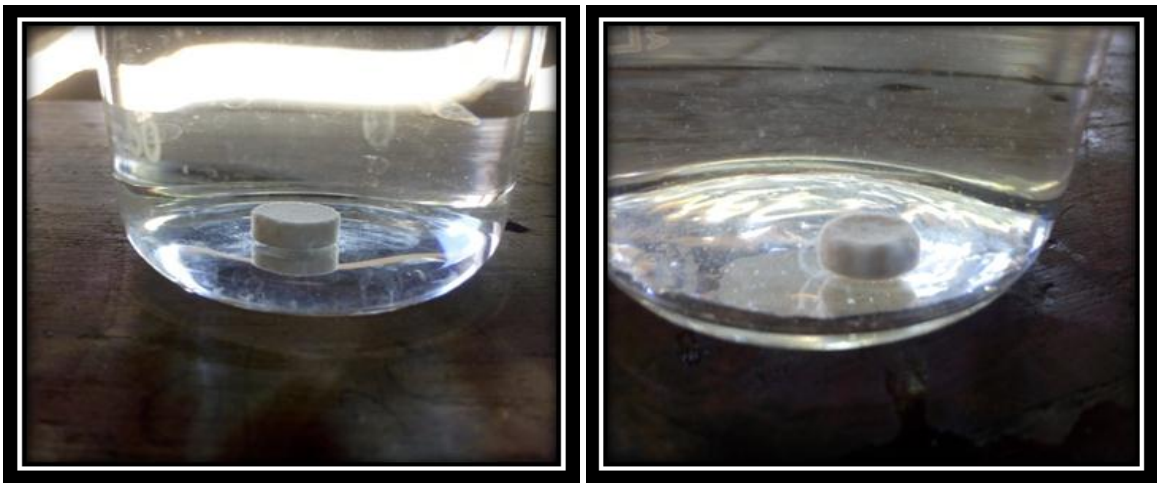
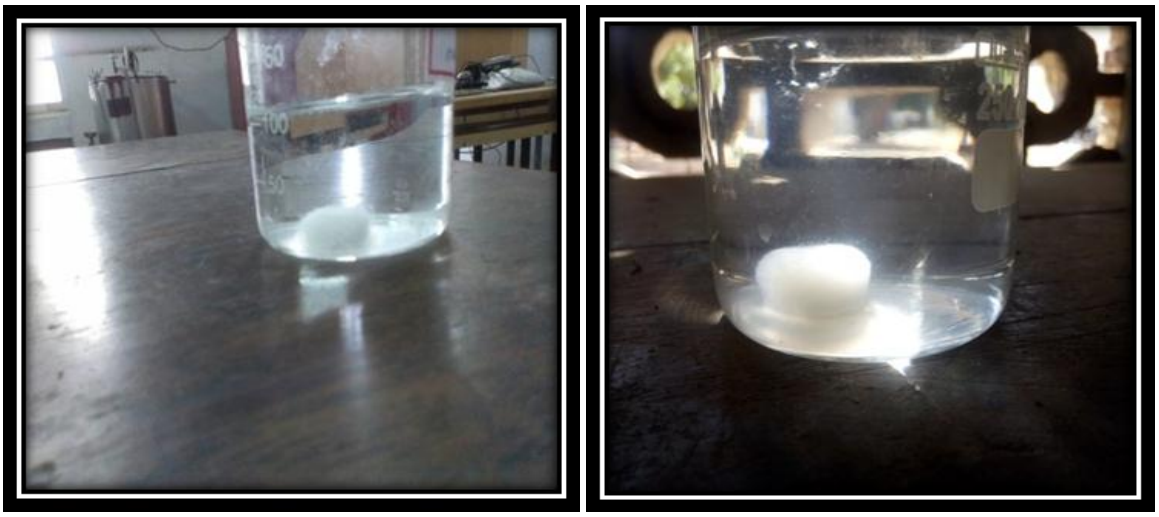


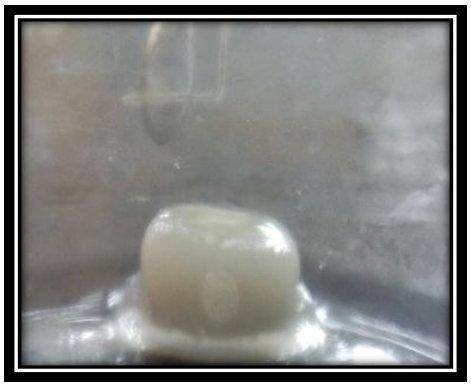
FIG.11: Swelling Index For All Formulations (F1-F10) Using 0.1N Hcl, Distilled Water and Acidic Buffer pH 2.2.



0hrs-2hrs



4hrs-6hrs



8hrs

FIG.12In-Vitro Swelling Behaviour of Best Formulation (F4) Using 0.1N Hcl.

FIG.13A IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING 0.1N HCl

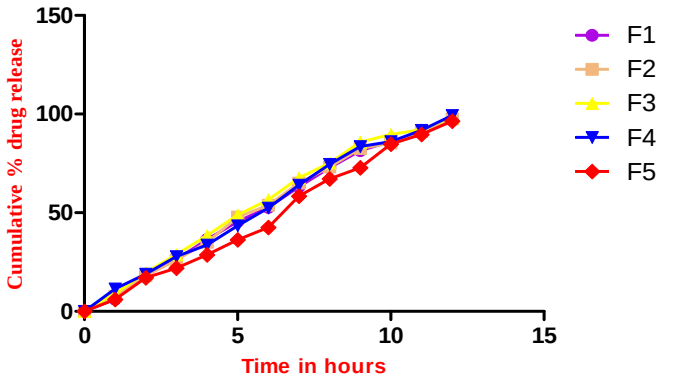


FIG.13B IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING 0.1N HCl

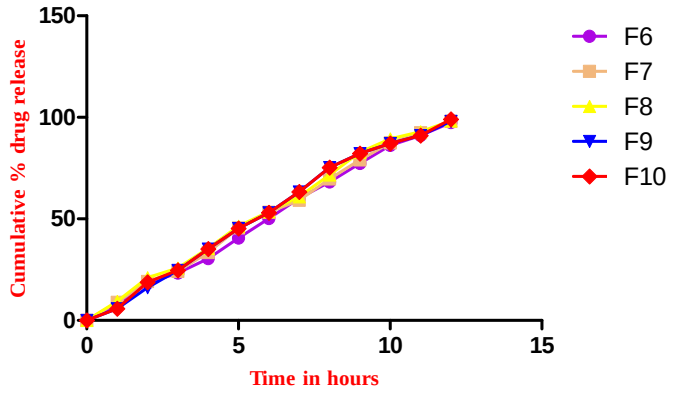


FIG.13C IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING DISTILLED WATER

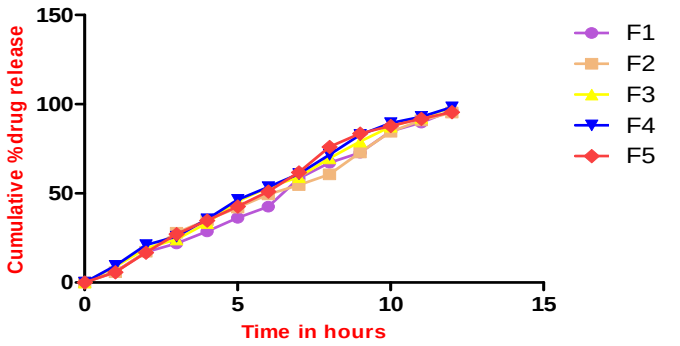


FIG.13D IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING DISTILLED WATER

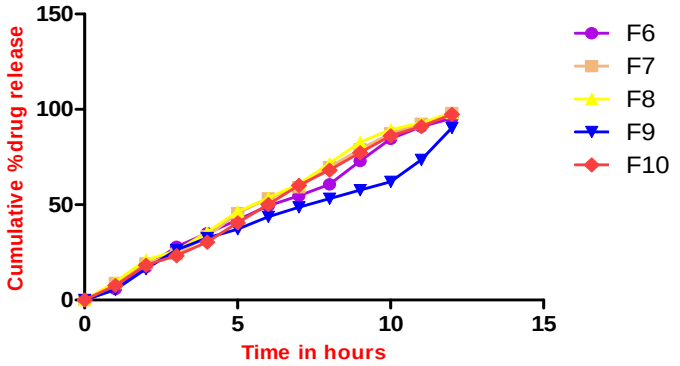


FIG.13E IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

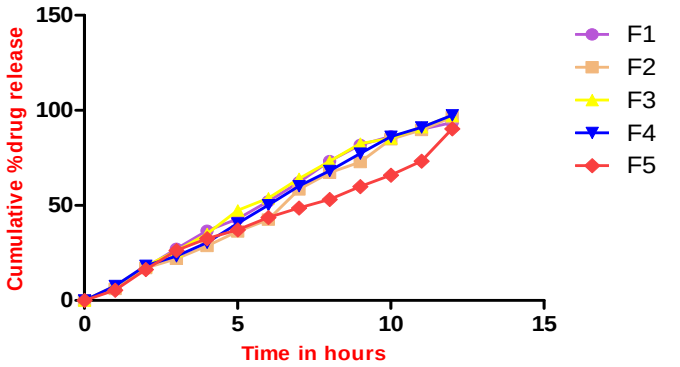


FIG.13F IN-VITRO DRUG RELEASE PROFILE OF PIRACETAM WITH DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

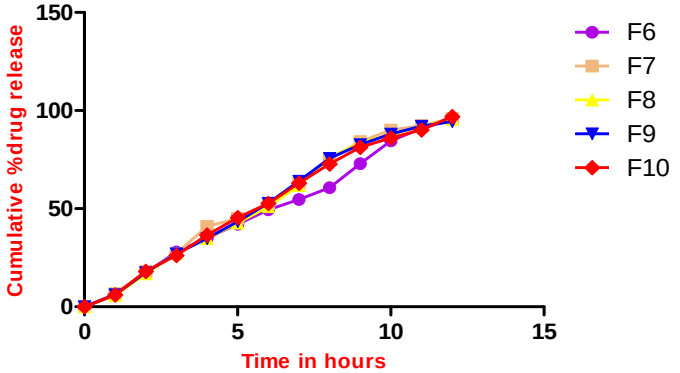


FIG.14A COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1NHCl

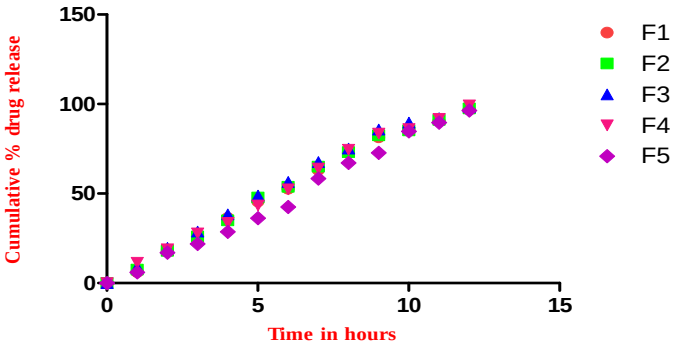


FIG.14B COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

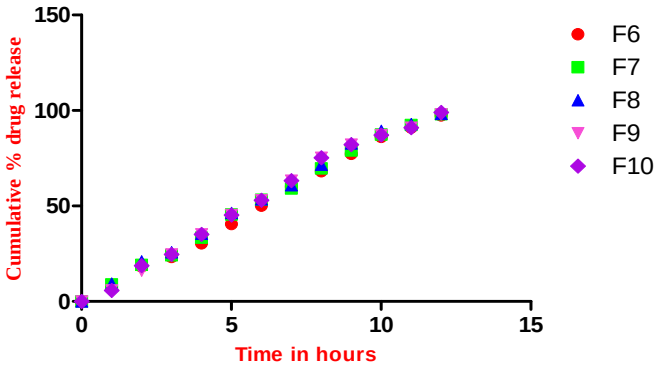


FIG.14C COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

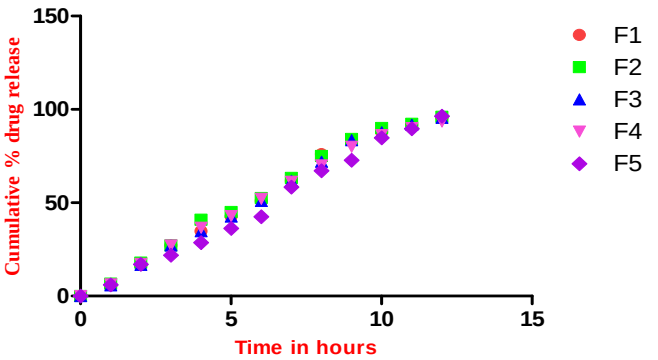


FIG.14 D COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

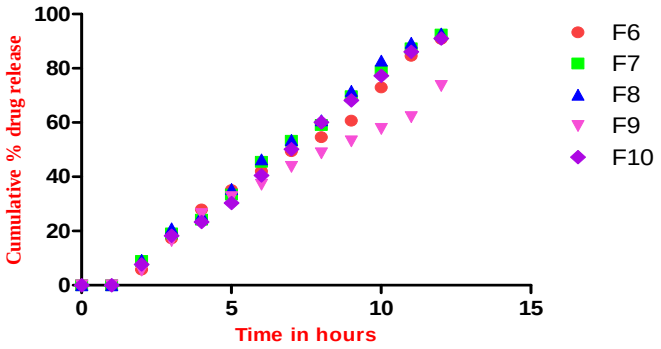


FIG.14E COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

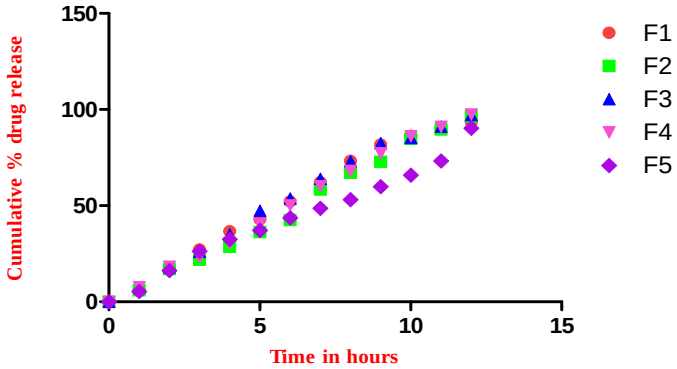


FIG.14F COMPARISION OF IN-VITRO ZERO ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

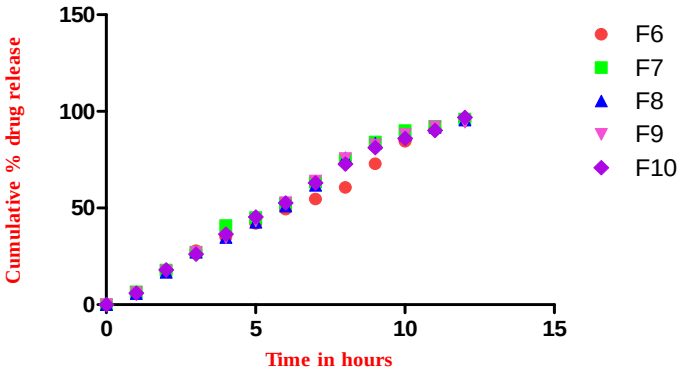


FIG.15A COMPARISION OF IN-VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1NHCl

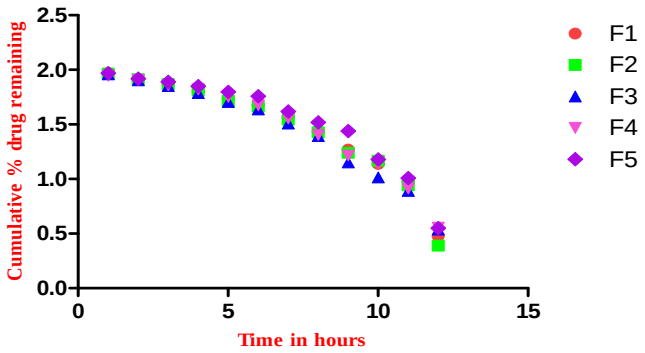


FIG.15B COMPARISION OF IN-VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1NHCl

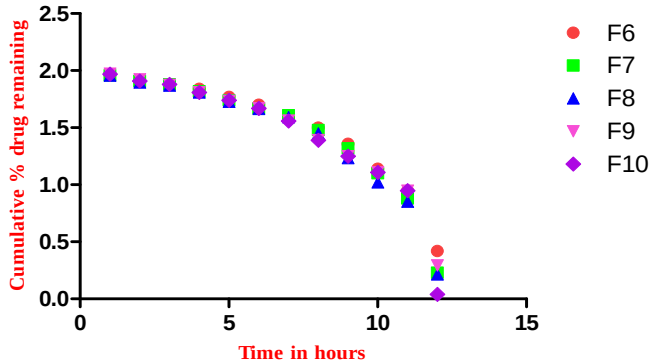


FIG.15 C.COMPARISION OF IN-VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

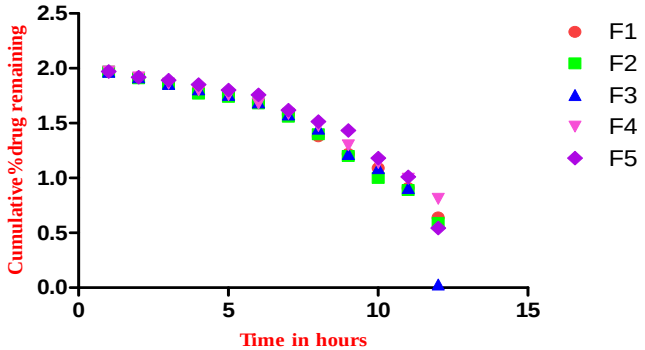


FIG.15 D COMPARISION OF IN VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

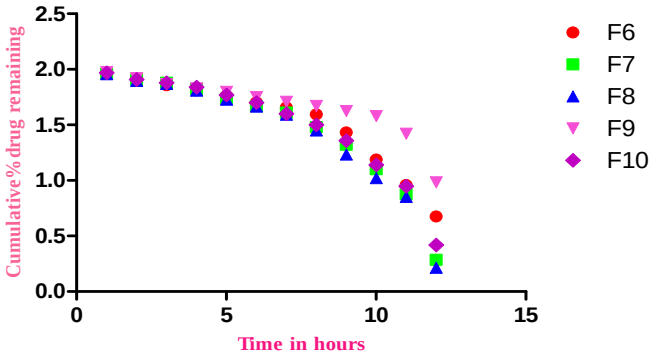


FIG.15 E COMPARISION OF IN VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

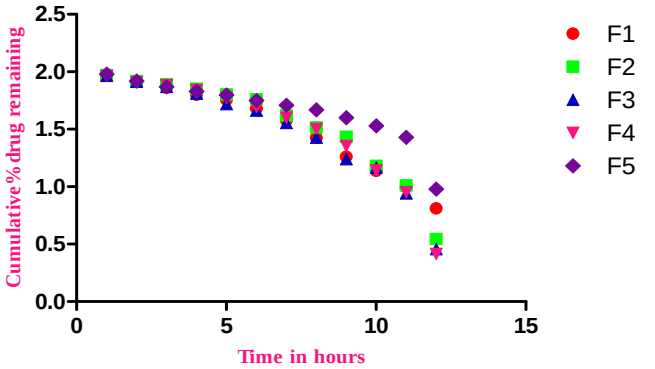


FIG.15F COMPARISION OF IN-VITRO FIRST ORDER RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

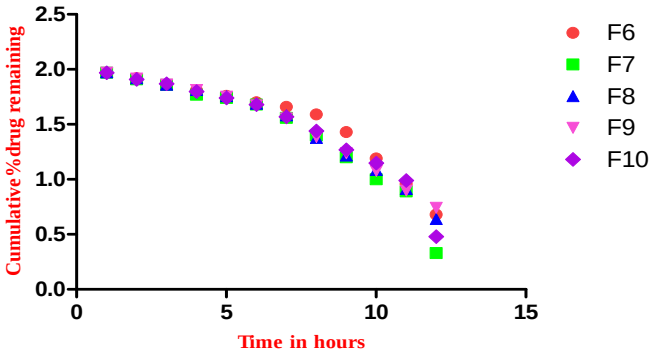


FIG.16A COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

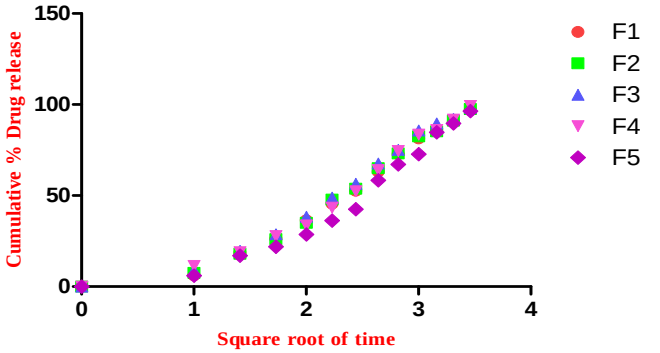


FIG.16B COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

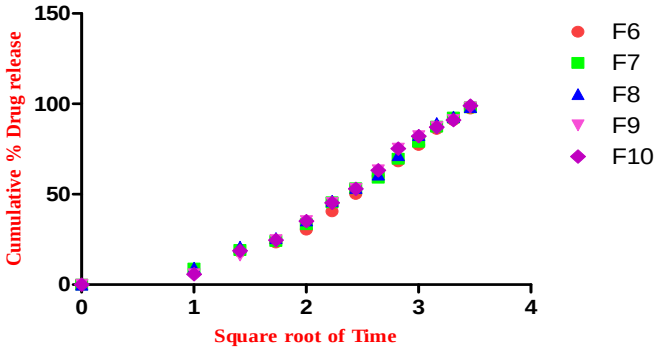


FIG.16C COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

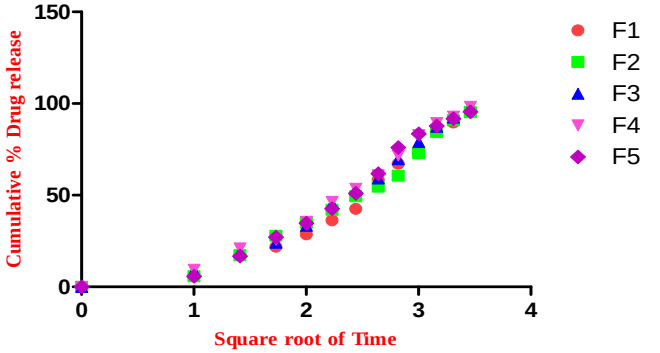


FIG.16D COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

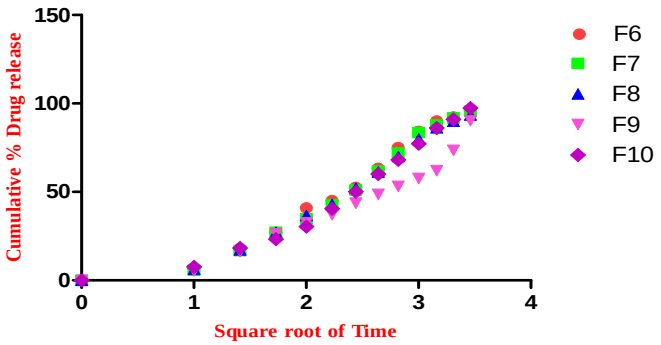


FIG.16E COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH2.2

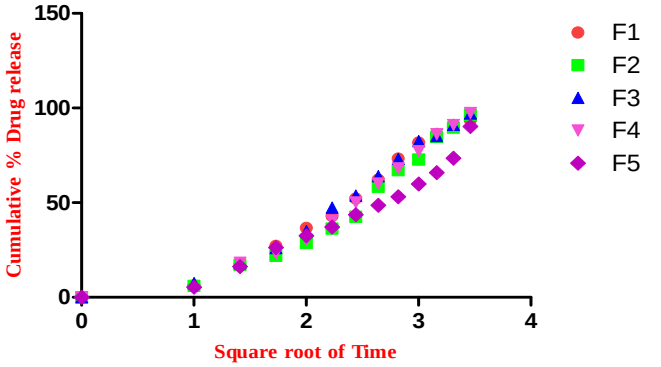


FIG.16F COMPARISION OF IN-VITRO HIGUCHI MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH2.2

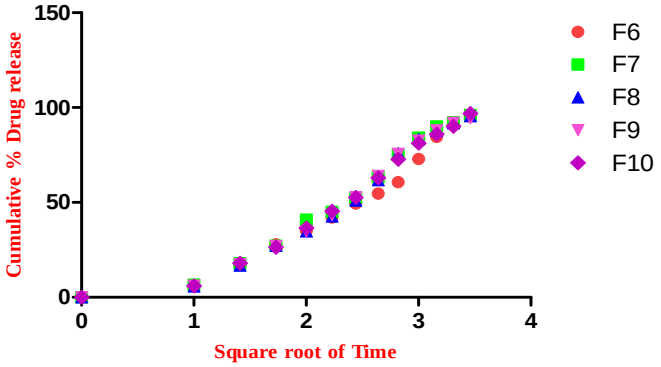


FIG.17A COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

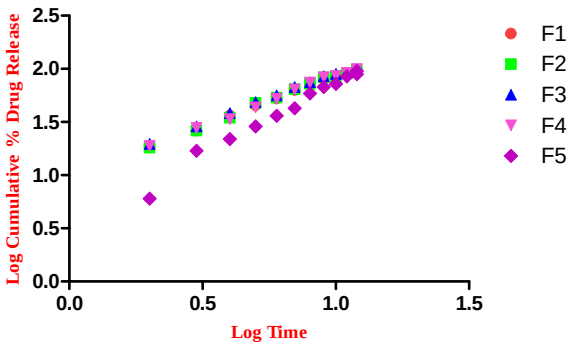


FIG.17B COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

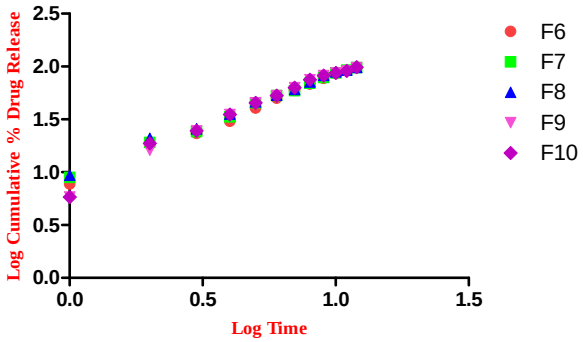


FIG.17C COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

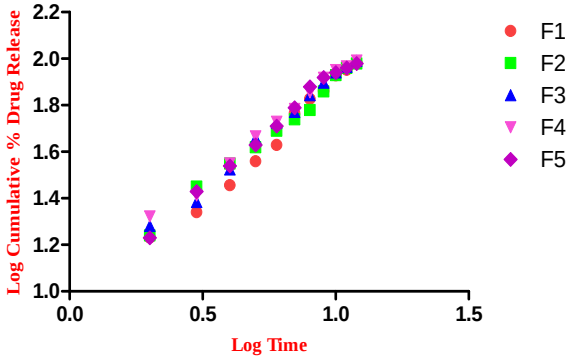


FIG.17D COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

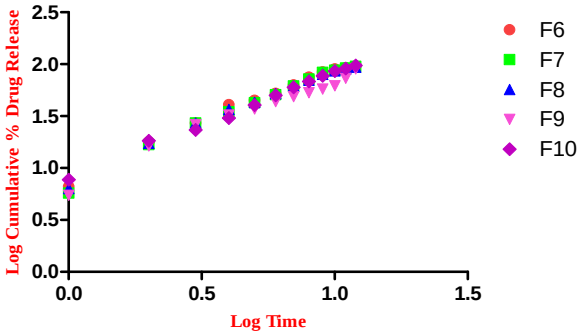


FIG.17E COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH2.2

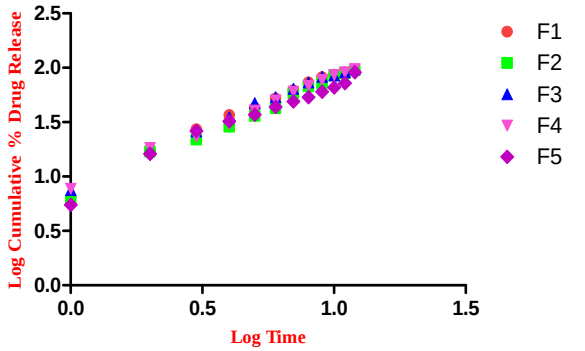


FIG.17F COMPARISION OF IN-VITRO KORSMEYER PEPPAS MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH2.2

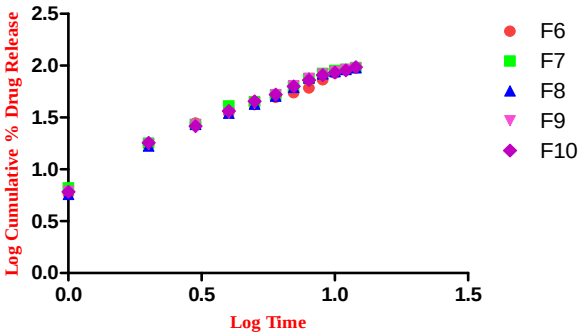


FIG.18A COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

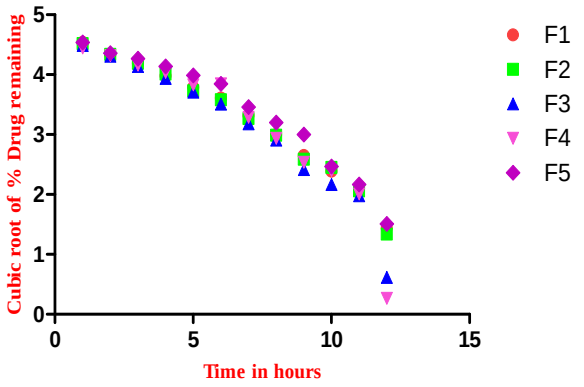


FIG.18B COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING 0.1N HCl

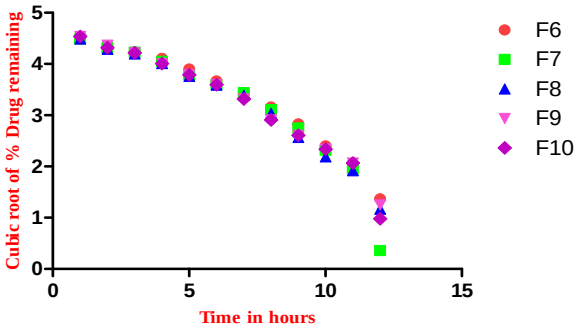


FIG.18C COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

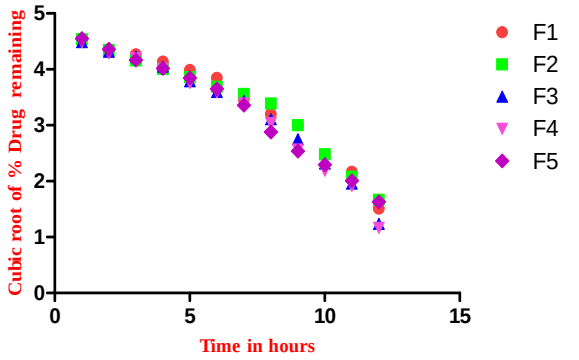


FIG.18D COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING DISTILLED WATER

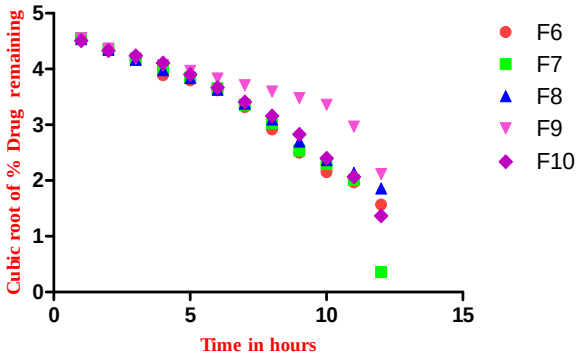


FIG.18E COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2

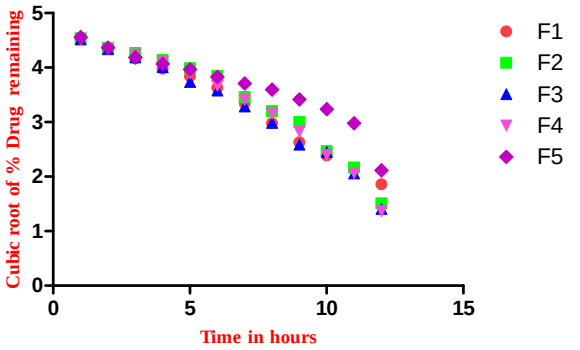
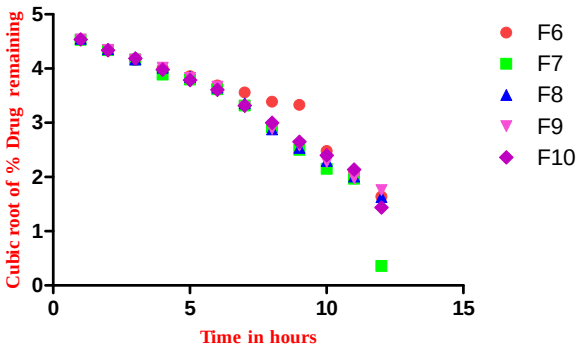
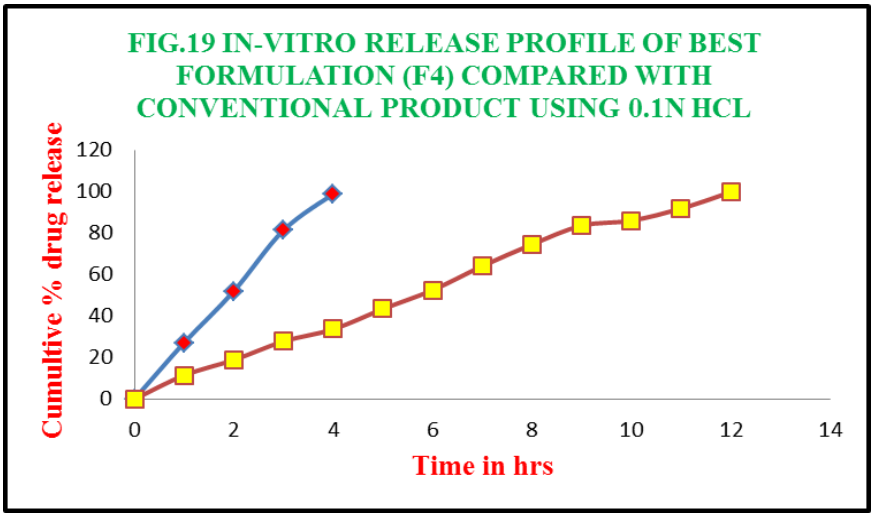


FIG.18F COMPARISION OF IN-VITRO HIXSON CROWELL MODEL RELEASE KINETICS OF FORMULATION CONTAINING DIFFERENT POLYMERS USING ACID BUFFER pH 2.2





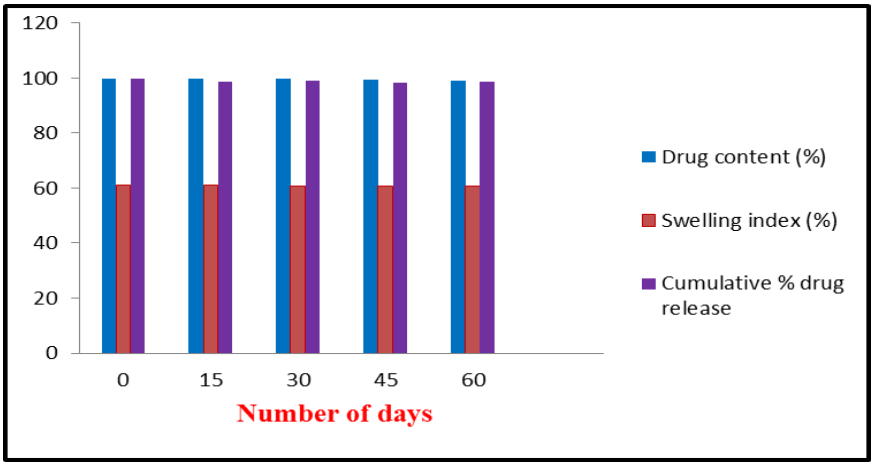


FIG.20: Drug Content, Swelling Index and Cumulative % Drug Release of Best Formulation (F4) Before and After Storage kept in Stability At 40°C /75%RH.

IV. SUMMARY AND CONCLUSION

SUMMARY

In present work attempts have been made to formulated controlled release matrix tablets of Piracetam by using natural & synthetic hydrophilic polymers, which is preferably used as ancognitive enhancer used in the treatment of Alzheimer's disease. Controlled release matrix tablets were prepared by using polymers such as HPMC K-15M, Xanthan gum, SCMC in different concentration by wet granulation technique. Piracetam meets all the ideal characteristics to formulated as matrix type controlled release drug delivery system.

Piracetam is a highly effective cognitive enhancer used as a model drug to develop a controlled release formulation. Piracetam exhibits pH dependent solubility. It is more soluble in acidic pH and slightly soluble at neutral or alkaline condition (intestinal environment).

- The λmax of Piracetam was found to be 201nm in 0.1N hydrochloric acid.
- The Piracetam obeys the Beer's law within the concentration of 5 to 25µg/ml.
- FTIR studies showed that there was no interaction between drug and polymers.
- The Controlled release matrix tablets were prepared by wet granulation method using different concentrations of gel forming natural & synthetic hydrophilic polymers.
- The formulated tablets were analyzed for pre compression and post compression parameter, swelling index, *in-vitro* drug release studies, *in-vitro* kinetics.
- The pre compression parameters of all the formulations were within the required limits was indicated good flow property, suitable for formulation of the tablets.
- The post compression parameters such as thickness, hardness, friability, uniformity of content and swelling index of all formulations were within the acceptable limits.
- F4 formulation was selected as best formulation based on in-vitro release studies, swelling studies, in- vitro release kinetics. The extent of drug release was found to be 99.75% in 12hrs.
- The drug release model of this formulation (F4) complies with zero order kineticsfollowed by Non-fickian diffusion mechanism.
- FTIR of selected best formulation shows that no interaction between the drug and polymers.
- Selected formulation showed controlled release profile than the conventional tablet (F14).

CONCLUSION

The results conclusively demonstrated that controlled release matrix tablets of Piracetam was effectively prepared by wet granulation method with desired properties and exhibited better in-vitro drug release profiles. The formulation F4 containing Xanthan gumexhibit maximum rate of drug release. So, this formulation was considered to be the optimized formulation. The developed controlled release matrix tablets of Piracetam may be used for prolonged drug release, thereby improving the patient compliance over other dosage forms.

The optimized formulation of Piracetam (F4) was selected. This controlled release matrix tablets were investigated under stability test 40^{o}C/75%RH for 2 months. From these data, the formulations were found to be stable under the conditions mentioned before since there was no significant changes in the percentage amount of drug content. Formulation F4 did not show any significant changes in appearance, hardness, swelling index, drug content, in-vitro

dissolution profile after 2 months. Thus, it was found that the optimized formulations, F4 were stable under these conditions for 2 months.

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