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PREPARATION AND EVALUATION OF VIGABATRIN MICROSPHERES MICROSPHERES LOADED WITH SAXAGLIPTIN

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ABSTRACT

Microspheres drug delivery system have used to improve patient compliance,decrease toxicity and increase efficacy. also, the use of microspheres to deliverthe drugs has manyother standards, like manage medication release, improve bioavailability, and direct drug delivery to the desired site. Microsphereformulations have advantage over conventional tablet or capsule formulations, since it increases the surface area exposed to the drug's absorption location, resulting in increased drug absorption and decreased drug dosage persistency.in this research work an effort was made to formulate microspheres of vigabatrin by using different natural polymers, in the ratios of (1:1,1:2,1:3),Vigabatrin is an Anti-Epileptic or Anti-Convulsant drug used to treat epilepsy and infantile spasms Vigabatrin is thought to work by stabilizing the electrical activity in your brain and calming it.prepared formulations are characterized for FTIR study, flow properties," critical angle of repose,tapped density,bulk density,hausner ratio,cars index (14.58±2.78)". yield of percentage (96.92), percentage of drug entrapment(97.58), theoretical drug content, practical drug content (97.28), in-vitro dissolution, kinetics of drug. formulation which passes all the evaluation parameters was considered as best formulation of vigabatrin.

Keywords:

Microsphere, ionotropic gelation, vigabatrin, microencapsulation, karaya gum.

Introduction

The most common, practical, and comfortable method of deliveringactivedrugstothebodyisorally administered pharmacological dosage forms. The most widely used medication delivery method is the oral Controlled release method because it has a number of advantages overtraditional methods like: Increased patient convenience and compliance, Lessvolatility in steady state plasma levels, which aids in improved illness condition management, Optimum medication use allowing for a decrease in total dose given, Lower medical expenses due to more effective treatment, less frequent dosage.

Controlled Drug Delivery

One of essential issues of drug formulation is the Controlled release of drugs, which can improve therapeutic efficacy by offering prolonged in vivo action, Controlled blood concentration as well as tissue-targeted local release. A probable approach to the integration of drug molecules into the biodegradable polymer microspheres is necessary for controlled and sustained release of medications.Controlled drug delivery occurs when a polymer, whether natural or synthetic, is prudently combined with a drug or other active agent in such a way that the active agent is released from the material in a predetermined manner. The purpose behind controlling the drug delivery is to attain more effective therapies while eliminating the potential for both under and overdosing. Other merits of using controlled-delivery systems can include the maintenance of drug levels within a desired range, reduced administration frequency, optimum drug use, and improved patient compliance. while these advantages can be significant, the potential disadvantages cannot be ignored the possible toxicity or Non biocompatibility of the components utilised, undesired degradation by products, any surgery needed to install or remove the system, and the possibility due to the delivery system's potential for causing patient discomfort and the more expensive controlled-release methods when compared to conventional pharmaceutical of patient discomfort due to the delivery device, and the higher cost of controlled-release systems compared with traditional pharmaceutical formulation

MATERIALS AND METHODS

Preparation of Microspheres

To create the dispersion, thecorrectamount of natural polymerslike Xanthan gum, guar gum, karaya gum was dissolved in 25ml of distilled water separately in different ratios(drug: polymers), and agitated. The vigabatrin(drug) wasadded to the polymer dispersionand mixed once more for homogenous distribution. And was combined with Vigorous stirring by using stirrer. A23G syringe needle was used to extrude the sodium alginate mixture into a calciumchloride solution (1percentage w/v). To increase the beads mechanical strength, they were left in the same solution for 30 minutes. Then created beads wereseparated, cleaned with water, and left to air dry for the entire day, Different ratios mentioned in below tab:1.

Components (mg)	VF1	VF2	VF3	VF4	VF5	VF6	VF7	VF8	VF9
Vigabatrin	500	500	500	500	500	500	500	500	500
Sodium Alginate	250	500	750	250	500	750	250	500	750
gum (Xanthan)	250	500	750	-	-	-	-	-	-
gum (Guar)	-	-	-	250	500	750	-	-	-
gum (Karaya)	-	-	-	-	-	-	250	500	750
(Drug: polymer)	1:1	1:2	1:3	1:1	1:2	1:3	1:1	1:2	1:3
Cacl2 (gm)	1	1	1	1	1	1	1	1	1

Tab:1. quantity of drug (different formulation) and polymers (different ratios)

EVALUATION OF PREPARED MICROSPHERES

Flow Properties

Bulk Density: A sample of microspheres which is correctly weighed was carefully introduced into a 10 ml graduated cylinder with the help of tube or conduit. The starting volume was usually noted. Carefully level the microspheres without compacting, if necessary, and read the unsettled apparent volume V_0, tothe nearest graduated unit. Calculate the bulk density in g/cm^3 by the formula.

$$D_f = M/Vo$$

Where D_f is bulk density,

M is weight of samples in grams and, V_0 is volumes of sample in cm^3.

Tapped Density: The tapped density was obtained by dividing the mass of a powder by the tapped volume in cm. A graduated cylinder with a 10 ml capacity is carefully filled with the microsphere sample.100 times from a height of 1 inch, the cylinder was dropped at 2-second intervals onto a firm wood surface. By dividing the sample weight by the formulation, the tapped density of each formulation was then determined. By dividing the sample's final tapped volume (in cm3) in cm3 by its weight in grammes. It was calculated by using equation given below

$$Do=M/V_t$$

Do= Bulk density,

M=weight of samples in grams

V_t=final tapped volumes of granules.

Critical Angle Of Repose: Critical angle of repose of a granular material is a steepest angle descent or dip relative to the horizontal plane to which a material can be piled without slumping, at the angle, the material on the slope face is on the verge of sliding

Hausnners Ratio: Hausner ratio of microspheres was calculated according to equation given below (USP NF 2007).

$$\text{Hausners ratio} = \text{tapped density/bulk density}$$

Where V_0 is bulk density and V_f is tapped density.

Carrs Index: The compressibility index and the hausner ratio are determined by measuring both bulk volume and tapped volume of microspheres. According to the equation shown below, the % compressibility of microspheres was computed.

$$\%\ \text{Compressibility Index} = \text{tapped density-bulk density/tapped density} \times 100$$

FTIR Study:FTIR spectroscopy was performed& The powders were compressed at 20 psi for 10 minutes on a KBr-press(automatic) to create the drug and potassium bromide pellets, and the spectra were scanned in the 4000-600cm-1 wave number range. Vigabatrin, polymers, Vigabatrinloaded microspheres, and blank microspheres were all the subjects of an FTIR investigation.

Estimation of Yield Percentage: The Percent(%) Practical Yield of Vigabatrin microspheres is determined to learn thepercentage yield or effectiveness of any process, which aids in choosing the best productionprocedure. The weight of Vigabatrin microspheres recovered from each batch in next of kin to the total starting material was estimated as the practical yield.Utilizing the formula, the prepared Vigabatrin microspheres' yield percentage was calculated.

$$\text{Percentage yield} = \text{practical yield /theoritical yeild} \times 100$$

Estimation of Percentage of Drug Entrapment:

The following formula was used to determine each batch's efficiency of drug trapping in terms of percentage drug entrapment:

PDE =Practical drug loading/theoretical drug loading×100

Theoritical Drug Content: Calculations were done to determine the theoretical drug content under the assumption that all of the Vigabatrin in the polymer solution being utilised gets trapped inside Vigabatrin microspheres and that there is no loss at any point throughout the construct of the microspheres.

Practical Drug Content: The basic procedure is used to determine actual drug content: Vigabatrin microspheres were weighed out and then dissolved in 100 ml of 0.1N HCL. The Vigabatrin microsphere in 0.1N HCL was completely dissolved in this solution after being left overnight. A concentration of 10 g/ml solution was created by filtering and further diluting this solution. In order to determine the amount of medication contained in the sample, the absorbance of the solutions was measured at 233 nm using a double beam UV-Vis and compared to a blank solution of 0.1 N HCL.

Invitro-Dissolution-Study:

The USP XXIII equipment was used to calculate the release rate of Vigabatrin microspheres using the rotating basket method. 900 cc of 0.1N HCL were used for the dissolution test, which was conducted at 50 rpm at 370.5°C. To prevent the microspheres from floating, vigabatrin was placed in a basket. For a period of 12 hours, a sample (5 ml) of the solution was taken out of the dissolution device hourly and replaced with new dissolution media. The samples were run through Whatmann filter paper, and at 233 nm, the solutions' absorbance was measured. The drug release versus time plot was used to examine the dissolution profiles of the formulations. To comprehend the release process, kinetic analysis of the acquired data was also applied.

Drug Kinetics: The cumulative release data were fitted to models representing zero order (Q v/s t), first order Higuchi's square root of time (Q v/s t1/2), [Log(Q0-Q) v/s t], and Korsemeyer Peppa's double log plot (log Q v/s log t) in order to examine the drug release kinetics and mechanism. Q is the cumulative % of drug released at time t and (Q0-Q) is the cumulative in four kinetics models of data treatment, the outcomes of in vitro release tests were plotted, in brief, as follows: Drug release cumulative percentage against time (zero order ratekinetics), Time-log cumulative proportion of medication kept (first order rate kinetics), Drug release cumulatively as a percentage vs time (Higuchi's basic diffusion equation), Drug release cumulative percentage logarithm vs time log (Peppas exponential equation).

RESULTS And Discussion

FTIR- Study

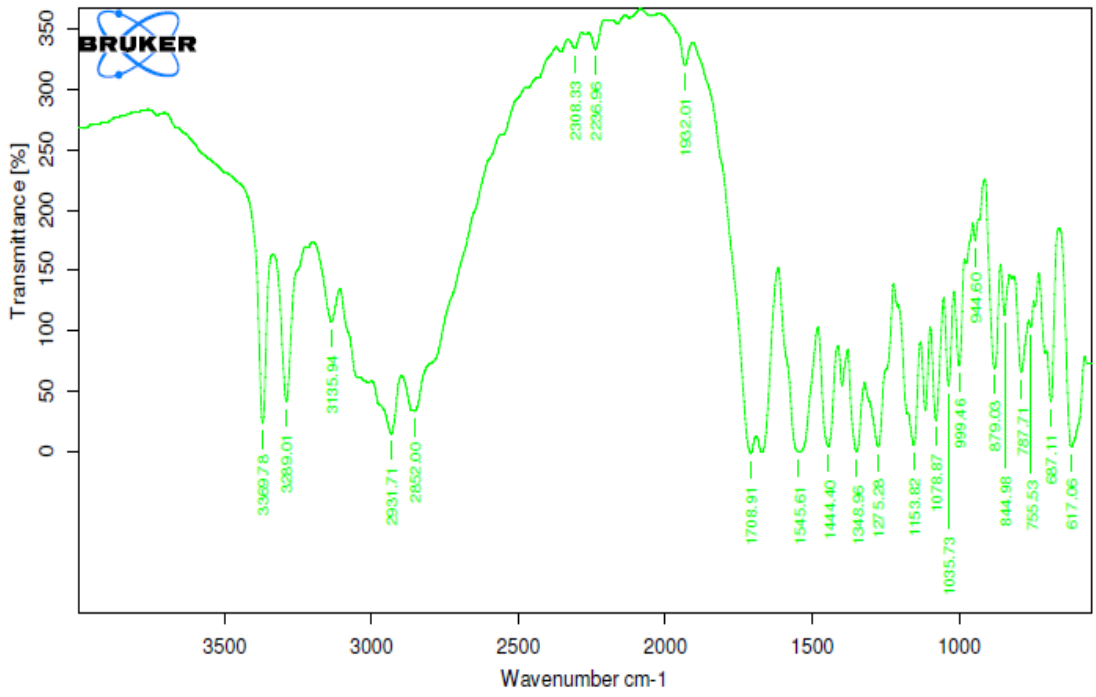

Fig:1 Result from FTIR-study (IR Spectra pure vigabatrin)

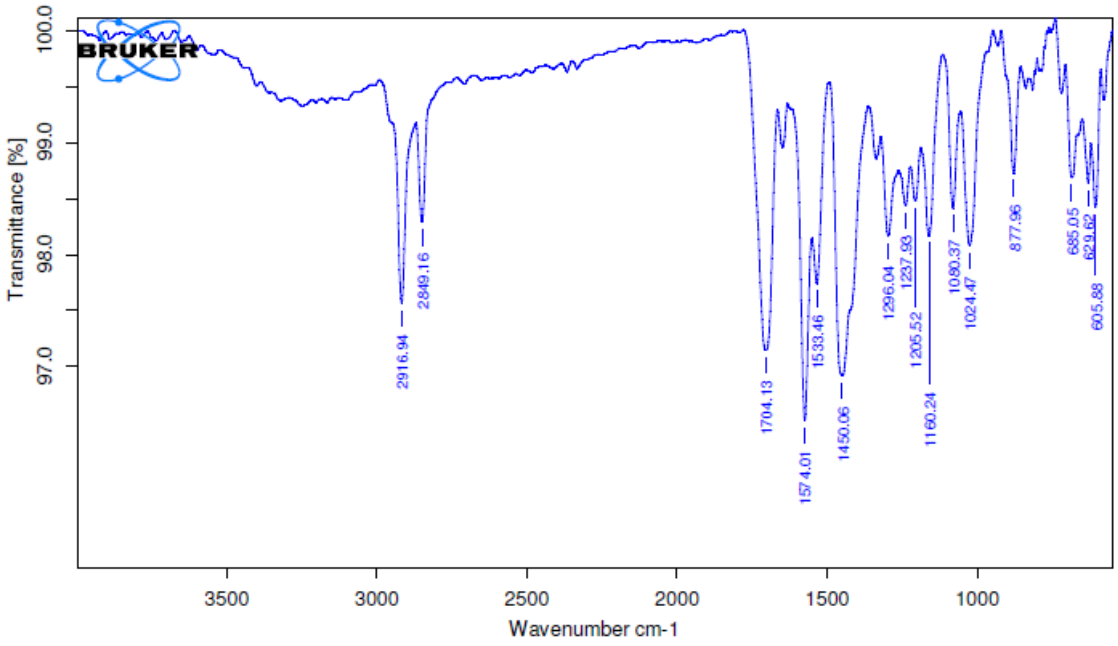

Fig:2. Result from FTIR-study (optimized formulation IR Spectra)

Flow Properties

Formula Code	Derivedproperties		Properties of flow		
	Bulk density (mean ±SD)	Tapped density(mean± SD)	Critical angle of repose	Carr's index (mean±SD)	Hausnners ratio (mean±SD)
VF1	0.36±0.04	0.42±0.012	25.02±0.30	14.28±1.96	1.16±0.02
VF2	0.39±0.012	0.47±0.04	26.25±0.39	17.02±1.94	1.20±0.06
VF3	0.38±0.012	0.44±0.06	27.81±0.64	13.63±3.92	1.15±0.05
VF4	0.39±0.016	0.46±0.012	26.36±0.96	15.21±1.76	1.17±0.02
VF5	0.39±0.06	0.46±0.06	31.74±0.73	15.21±2.22	1.17±0.03
VF6	0.41±0.05	0.47±0.008	28.96±0.36	12.76±3.18	1.14±0.05
VF7	0.40±0.025	0.46±0.021	30.72±0.29	11.12±1.16	1.15±0.02
VF8	0.40±0.06	0.45±0.014	32.80±0.40	11.12±3.64	1.12±0.05
VF9	0.41±0.04	0.48±0.022	34.44±0.34	14.58±2.78	1.17±0.04

Tab:2. Result from flow properties

S.No	Formulation Code	%(Yield (%)	Percentage Drug Content	Drug Entrapment (%)
1	VF1	70.64	90.10	89.16
2	VF2	74.42	92.62	90.22
3	VF3	79.19	94.62	93.78
4	VF4	76.41	94.96	93.26
5	VF5	80.46	97.82	95.82
6	VF6	84.62	98.83	97.68
7	VF7	80.72	97.16	94.62
8	VF8	84.74	97.19	96.29
9	VF9	96.92	97.58	97.28

Tab:3.Results from percentage yield,drug content,drug entrapment

In-Vitro Dissolution Study

Time (hrs)	VF1	VF2	VF3	VF4	VF5	VF6	VF7	VF8	VF9
0	0	0	0	0	0	0	0	0	0
1	22.42	16.42	14.26	24.82	20.12	19.24	20.24	18.56	14.76
2	34.24	30.02	21.92	36.26	34.81	26.78	36.64	24.71	24.72
3	38.92	38.24	30.68	51.84	51.84	38.86	48.81	36.81	36.42
4	55.18	46.36	44.84	66.86	62.89	44.68	56.60	48.87	42.46
5	64.69	54.26	53.62	79.92	74.02	52.96	68.98	54.82	46.58
6	72.26	68.61	66.86	88.86	82.46	68.48	74.89	75.46	52.82
7	90.28	74.65	78.42	99.86	94.18	74.18	88.21	78.84	66.77
8	94.12	88.96	80.98		97.28	86.64	97.64	86.76	78.21
9		92.26	89.63			92.98		92.92	82.48
10		94.62	92.76			99.14		96.28	88.46
11			96.01						92.49
12									99.92

Tab:4.in vitro release vigabatrin microspheres data

Result From Drug Kinetics

Zero - Order - Release

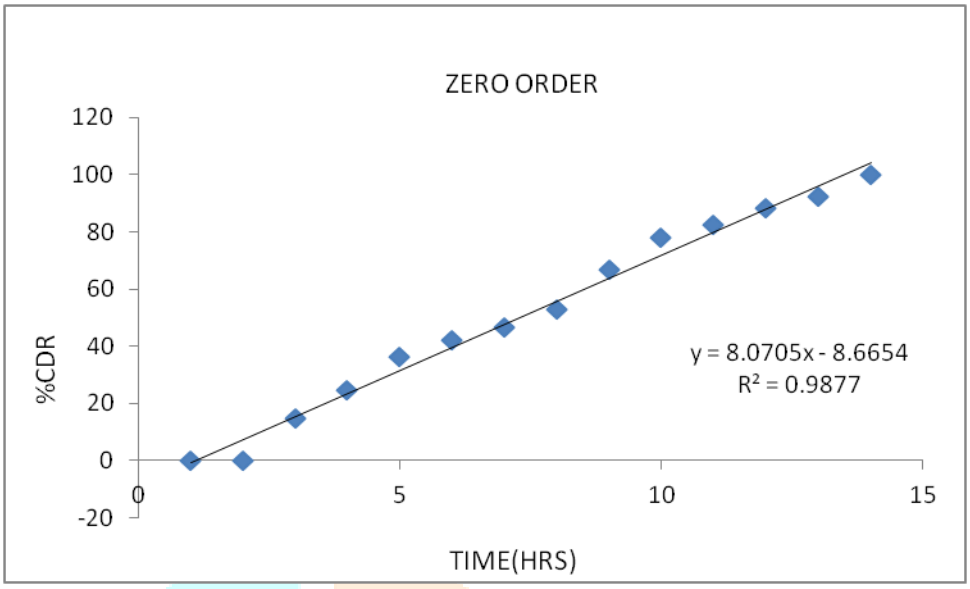

Fig:3. Zero -Order -Release graphof Vigabatrin superlative formulation (VF9)

First -Order -Release

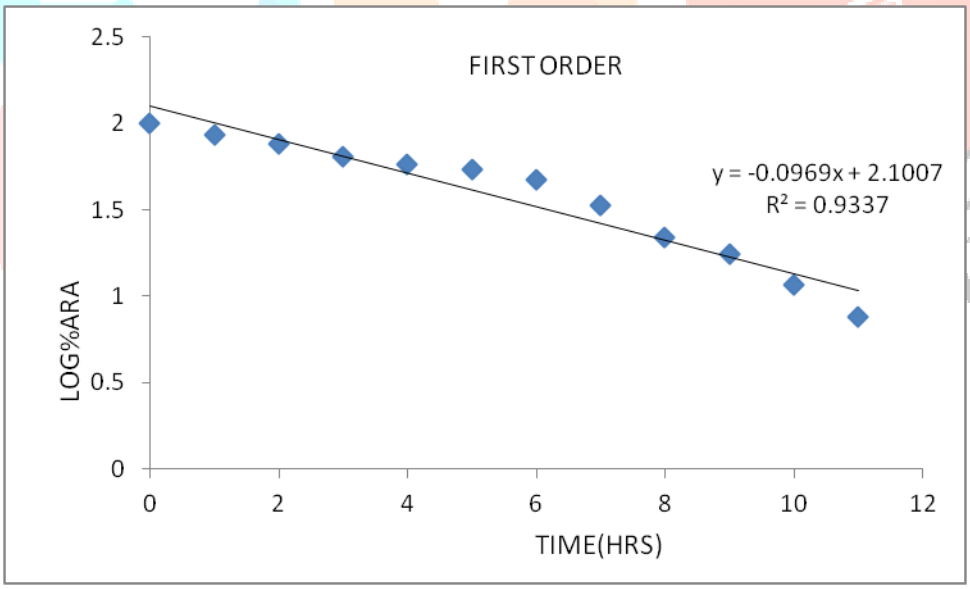

Fig:4. First -Order -Release graphof Vigabatrin superlative formulation (VF9)

Release Graph of Higuchi

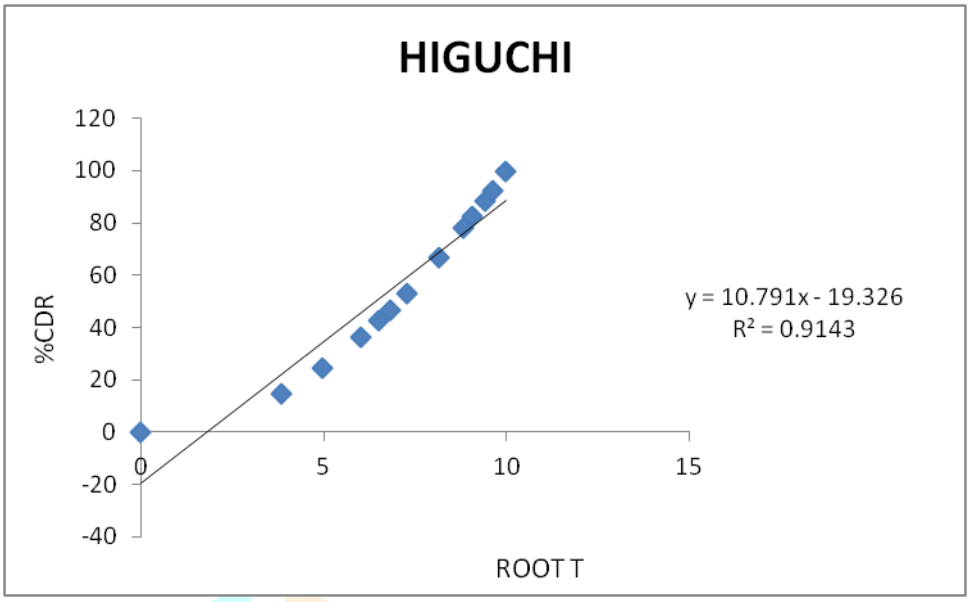

Fig:5.Release Graph of HiguchiofVigabatrin superlative formulation (VF9)

Peppas Release Plot

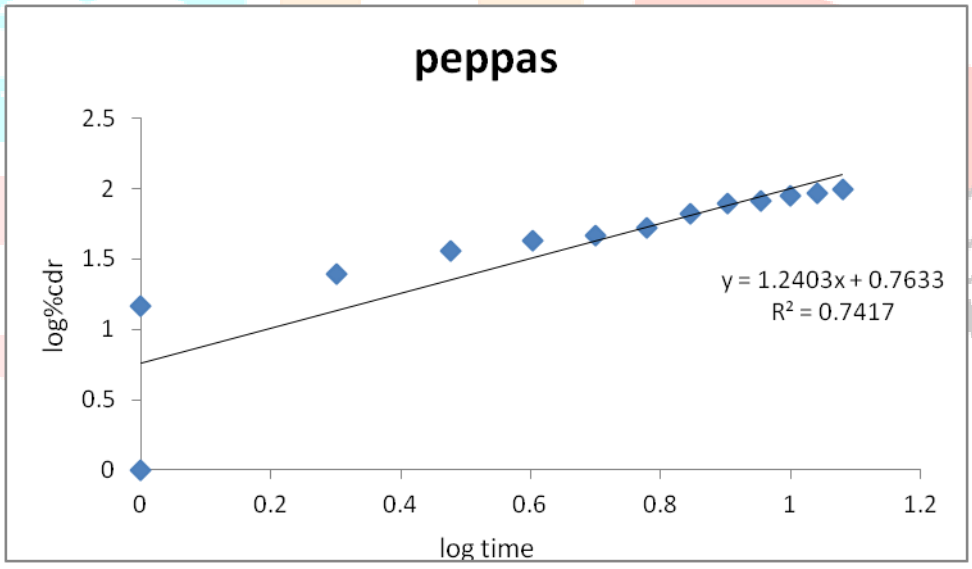

Fig: 6. Peppas release kinetics graph of Vigabatrin superlative formulation (VF9)

Formulation	Zero–order	First-order	Higuchi - Matrix	Peppas -plot	
				r^2value	n- value
VF9	0.987	0.933	0.914	0.741	1.240

Tab:5. Valuesfor the regression coefficient (r2) Microspheres ofvigabatrin

T

he Vigabatrin microspheres display Zero order drug release with a super case II transport mechanism, according to the drug release kinetic tests.

CONCLUSION

The objective of the current study is to deliver a therapeutic dose of (Vigabatrin) to the appropriate location in the body as well as to reach and maintain the desired Vigabatrin concentration.In an effort to develop an oral controlled release of the medication, microspheres of Vigabatrin were prepared utilising ionic gelation techniques and polymers such xanthan gum, guar gum, and karaya gum. In the current investigation, nine formulations were created utilising different amounts of xanthan gum, guar gum, and karaya gum.Shimadzu UVspectrophotometer was utilised in the Pre-formulation study to evaluate the concentration of vigabatrin at a maximum of 233nm using 0.1 N HCL as a buffer. This approach had good consistency and was applied throughout the entire investigation.All of the compositions underwent examination. FTIR study, percentage (%) yield, percentage (%) drug, sinking time & entrapment efficiency, in-vitro dissolution & release kinetics,& pre-formulation experiments' results all showed positive results.There has been no association with polymers & vigabatrin, according to the FTIR spectra. Increased polymer concentration resulted in greater entrapment effectiveness. The findings suggest that Vigabatrin was distributed properly in the microspheres, and the variation was within acceptable bounds.Due to the general high polymer concentration, composition VF9 demonstrated a good sustained release characteristic with maximal entrapment efficiency based on release data & graphical analysis. -The release data was better suited with zero -order -kinetics, according to the co-efficient of assessment. The mechanism of diffusion Controlled release is explained by the Higuchi equation. For the Vigabatrin microspheres synthesised with drug &karaya gum, the diffusion exponent 'n' values of the Korsemeyer- Peppas model were determined to be in the range of greater than 1, confirming super case 2 transport diffusion mechanism of drug through Vigabatrin microspheres.Accordingly, utilising the ionic gelation process and polymers such xanthan gum, guar gum, karaya gum, it is possible to create promising controlled release microspheres containing vigabatrin, By constantly releasing the drug over a certain period of time, the idea of creating microspheres containing vigabatrin offers an appropriate, practical strategy to provide a sustained therapeutic impact.in the current study, various polymers were used successfully to create vigabatrin microspheres by the ionotropic gelation process.

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