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Research Article

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Formulation and evaluation of sustained release microbeads of Venlafaxine hydrochloride using various polymers.

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Abstract

The main aim of the study is to formulate Venlafaxine Hydrochloride loaded microbeads of sodium alginate using gelatin and pectin as release modifiers by Ionotropic Gellation Method. The microbeads were prepared by varying the concentration of sodium alginate, gelatin and pectin. The drug – polymer compatibility was studied by FTIR studies. No significant drug-polymer interaction were observed in FTIR studies. The prepared microbeads were evaluated mainly for the Sustained Release of the drug apart from the other tests like swelling ratio, particle size, drug entrapment, SEM, *in vitro* release study. Particle size distribution of the loaded formulations were measured by an optical microscope and particle size of optimized beads was determined by SEM. In vitro drug release profile of Venlafaxine Hydrochloride microbeads was examined in 0.1N Hydrochloric acid for first 2 hrs followed by pH 7.4 phosphate buffer for 8 hrs. The formulated beads had shown higher entrapment efficiency, drug loading, low particle size. The formulation F6 released Venlafaxine Hydrochloride for longer duration up to 10hrs.

Keywords: Venlafaxine Hydrochloride, Sodium alginate, Gelatin, Pectin , Microbeads, Ionotropic Gellation method, Sustained Release dosage form.

1. Introduction

Sustained release formulation [1-5]

Sustained release technology has emerged as an important new field in the development of pharmaceutical dosage form. Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. More precisely, sustained drug delivery can be defined as “Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable effects”.

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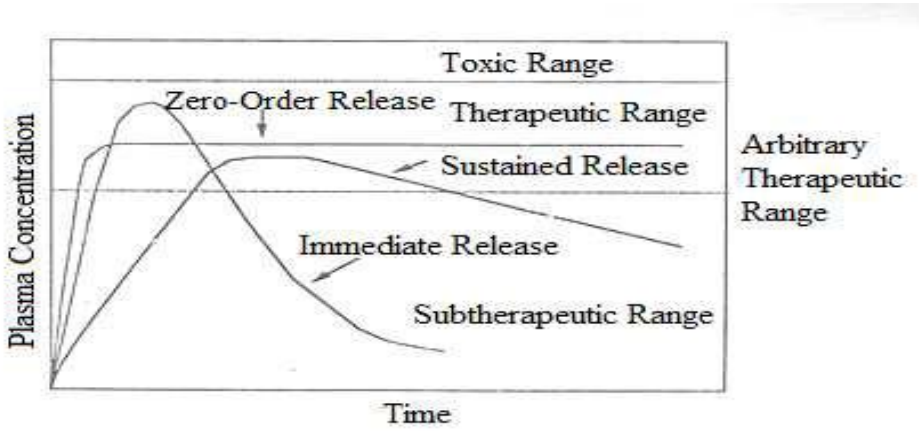

Fig.1 Plasma drug concentration profiles for conventional tablet formulation, a sustained release formulation and a zero order controlled release formulation.

In sustained release dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response. The remaining fraction is released periodically and is required to maintain the maximum initial pharmacological activity for some desirable period of time in excess of time expected from usual single dose. The onset of its pharmacologic action is the often delayed and the duration of its therapeutic effects is sustained. A sustained release is facilitated through the consistent rejuvenation of drug molecules.

By the sustained release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. The sustained plasma drug levels provided by sustained release products often eliminate the need for night dosing, which benefits not only the patients but the care given as well. The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutic, Pharmacokinetic and Pharmacodynamic properties of a drug in such a way that its unity is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most possible route.

Potential advantages and disadvantages of Sustained release drug delivery systems:

- Minimize or eliminate local side effects
- Minimize or eliminate systemic side effects
- Obtain less potentiating or reduction in drug activity in chronic use.
- Minimize drug accumulation with chronic dosing.

Sustained release drug delivery systems are also associated with some of the disadvantage like

- Dose dumping
- Reduced potential for dosage adjustment
- Increased first pass clearance
- Poor systemic availability in general

The various approaches or the novel drug delivery systems include: liposomes, microspheres, nanoparticles and microbeads.

Microbeads (or) Microspheres[5,6]

"Microbeads or Microspheres are defined as solid spherical particles containing dispersed drug in either solution or micro-crystalline form".

Microbeads or Microspheres are small spherical particles, with diameters in the micrometer range (typically 1 µm to 1000 µm). Microspheres are sometimes referred to micro- particles and micro beads. Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers. The range of Techniques for the preparation of microspheres offers a Variety of opportunities to control aspects of drug administration and enhance the therapeutic efficacy of a given drug.

Methods of preparation: [7-10]

Incorporation of solid, liquid or gases into one or more polymeric coatings can be done by microencapsulation technique. The different methods used for various microspheres preparation depends on particle size, route of administration, duration of drug release, method of cross linking, evaporation time and co-precipitation, etc. different preparation methods are:

- Single emulsion technique
- Double emulsion technique
- Solvent Evaporation
- Solvent extraction
- Spray Drying
- Hot Melt Microencapsulation
- Phase separation coacervation technique
- Spray drying and spray congealing
- Polymerization techniques

2. Experimental Methodology

Preparation of standard curves of venlafaxin hydrochloride:

Concentration of venlafaxine hydrochloride in the solution was estimated by stable beam spectrophotometer at 229nm. The standard curves were prepared in pH 1.2 Hcl and pH 7.4 buffer (Phosphate) solutions.

Preparation of Hcl buffer pH 1.2: 50ml of the potassium chloride solution (0.2M) was placed in a 200ml volumetric flask and to it was added 85ml of hydrochloric acid solution (0.2M) and then distilled water was added to make the volume to 200ml**.**

Preparation of buffer pH 7.4:

Dissolve 2.38gm of disodium hydrogen phosphate, 0.19 gm of potassium dihydrogen phosphate and 8.0 gm of sodium chloride in sufficient water to produce 1000ml.

Preparation of standard curve of venlafaxineHcl in 1.2 pH Hcl buffer:

Accurately weighed 50 mg of venlafaxine Hcl was dissolved in 50 mL of 0.1 N HCl (pH-1.2) (Conc. 1000 µg/mL). From this solution, 10 mL was pipetted out into 100 mL volumetric flask and volume was made up to with 0.1 N HCl (pH-1.2) (Conc. 100 µg/mL). Further 10ml aliquot was taken from this solution (100µg/ml) and diluted to 100ml with 0.1 N HCl (pH-1.2) to give 10µg/ml standard solution of drug.

Preparation of standard curve of Venlafaxine Hcl in Phosphate Buffer pH 7.4.

100 mg of Venlafaxine hydrochloride was accurately weighed and dissolved in simulated tear fluid (phosphate buffer pH7.4) in a 100 ml volumetric flask then the volume was made up to 100 ml with phosphate buffer pH 7.4. This was primary stock solution , containing 1000 µg/ml. From this primary stock solution 1 ml was pipetted out and transferred in to a 100 ml volumetric flask and volume was made up to 100 ml with phosphate buffer pH 7.4.which contained the concentration of 10 µg/ml (Second stock solution). From second stock solution aliquots equivalent to 2-10µg were pipette out in to a series of 10 ml volumetric flask and volume was made up to 10 ml with phosphate buffer pH7.4.The absorbances of these solutions were measured against the phosphate buffer pH 7.4 as blank at 229 nm using UVvisible double beam spectrophotometer . Then a calibration curve was plotted taking concentration in µg/ml on X-axis and absorbance on Y-axis.

Preparation of Alginate-Pectin Microbeads:

The drug loaded microbeads were prepared using optimized concentration of sodium alginate and Pectin as a coating polymer.To 50ml of deionized water, Pectin was added and stirred with the electric stirrer to form mucilage. Then sodium alginate was added to form uniform dispersion. Weighed quantity of venlafaxine was added and homogenized for 5 min. The resulting dispersion was dropped through syringe with needle into 100ml of 2%w/v aqueous calcium chloride solution and stirred at 100rpm. After stirring for 1 hour, the formed beads were separated by filtration, washed with distilled water, dried at 50^0C in an oven.

Preparation of Alginate–Gelatin Microbeads:

The drug loaded microbeads were prepared using optimized concentration of sodium alginate and gelatin as a coating polymer. To 50ml of deionized water, gelatin was added and stirred with the electric stirrer to form mucilage. Then sodium alginate was added to form uniform dispersion. Weighed quantity of venlafaxine was added and homogenized for 5 min. The resulting dispersion was dropped through syringe with needle into 100ml of 2%w/v aqueous calcium chloride solution and stirred at 100rpm. After stirring for 1 hour, the formed beads were separated by filtration, washed with distilled water, dried at 50^0C in an oven.

Formulation of Venlafaxine microbeads:

The venlafaxine microbeads were prepared by ionotropic gellation method. The microbeads were prepared using sodium alginate, pectin and gelatin as polymer and calcium chloride across linking agent. Total 6 formulations were finalized by incorporating concentrations of polymer and cross linking agent. The concentrations of drug along with other excipients were summarized in **table 1**

Table 1 Formulation of venlafaxine microbeads

Formulation code	Venlafaxine (mg)	Sodium alginate (mg)	Pectin (mg)	Gelatine (mg)	$Cacl_2$ (%)	Glutaraldehyde (ml)
F1	250	0.25	-	0.25	2	1
F2	250	0.3125	-	0.1875	2	1
F3	250	0.375	-	0.125	2	1
F4	250	0.25	0.25	-	2	1
F5	250	0.3125	0.1875	-	2	1
F6	250	0.375	0.125	-	2	1

Evaluation of Microbeads:[10 -15]

The prepared microbeads were evaluated by the following parameters

A) Particle size by optical microscopy.
B) Estimation of Percentage yield
C) Drug entrapment efficiency.
D) Scanning electron microscopic studies (SEM).
E) Swelling study.
F) *In vitro* drug release study.
G) Release kinetics.
H) Fourier transform infrared spectroscopy analysis.
I) Differential scanning calorimetric analysis.

A) Measurement of microbeads size by optical microscopy

Particle size of the prepared beads was determined using an optical microscope fitted with a stage and an occular micrometer. Mean diameter was calculated by measuring diameter of 50mg dried microbeads of each formulations.

B) Percentage Practical Yield

The yield of microbeads was determined by comparing the whole weight of microbeads formed against the combined weight of the copolymer and drug.

$$\% \text{ Practical yield} = \frac{\text{Mass of microbeads obtained}}{\text{Total weight of drug and polymer used}} \times 100$$

C) Estimation of drug entrapment efficiency (DEE)

Known amount of microbeads were added to 100 ml USP phosphate buffer of pH 7.4 for complete swelling at 37 ^{o}C. The beads were crushed in a glass mortar with pestle, the solution was then heated gently for 2 h to extract the drug completely and centrifuged to remove polymeric debris. The clear supernatant solution was analyzed for drug content using UV-visible spectrophotometer at 229 nm.

$$\text{Entrapment efficiency} = \frac{\text{Estimated \% drug content in microspheres}}{\text{Theoretical \% drug content in microspheres}} \times 100$$

D) Scanning electron microscopic studies (SEM)

The microbeads were mounted onto stubs using double sided adhesive tape and sputter coated with platinum using a sputter coater (Edward S 150, UK). The coated beads were observed under SEM (JEOL, JSM-6360, Kyoto, Japanatthe required magnification at room temperature. The acceleration voltage used was 10 kV with the secondary electron image as a detector.

E) Swelling study

The dynamic swelling behavior of the microbeads was studied by the 50 mg of beads were incubated with 25 ml phosphate buffer solution pH 7.4 at 37^{o}C. The beads were taken out at different time intervals and blotted carefully without pressing hard to remove the excess surface liquid. The swollen beads were weighed using the electronic microbalance. The percent water uptake (Q) at different time intervals was calculated.

F) *In-vitro* drug release study

In-vitro drug release study was carried out using a Dissolution Apparatus USP XIV-II. The dissolution medium was maintained at 37.0 ± 0.5 ^{o}C and 50 rpm speed. The dissolution medium consists of simulated intestinal fluid (pH 7.4 phosphate buffer) for 8 hours. At predetermined time 5ml aliquots were removed every 30mins and an equivalent amount of fresh dissolution mediun was replaced. The amount of drug released was analysed at 229nm spectrophotometrically.

G) Data analysis (curve fitting analysis)

To analyze the mechanism of the drug release kinetics of the dosage form, the data obtained were fitted to various kinetic equations of zero order, first order, Higuchi model and Korsmeyer - peppas model and plotted as:

1. Cumulative percent drug released Vs time(Zero order plots)
2. Log cumulative percent drug remaining Vs time(First order plots)
3. cumulative percent drug release Vs square root of time(Higuchi plots)
4. (percent drug release) 1/3 Vs time (Hixson crowell plot)
5. log cumulative percent drug release *Vs* log time(Korsmeyer-Peppas Plots)

Zero order kinetics:

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

$$Q_0 - Q_t = K_0 t$$

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, $Q_0 = 0$)
K_0 is the zero order release constant expressed in units of concentration/time.

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with slope equal to K_0.

First order kinetics:

The release of the drug which followed first order kinetics can be expressed by the equation:

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

Where, C_0 is the initial concentration of drug,
k is the first order rate constant
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.

Higuchi model:

The release of the drug which follows higuchi kinetics can be expressed by the equation:

$$Q = K_H * t_{1/2}$$

Where, K_H is the Higuchi dissolution constant
Q is the amount of drug released in time t

The data obtained were plotted as cumulative percentage drug release versus square root of time.

Hixson crowell model:

Hixson crowell recognized that the particle regular area is proportional to the cube root of its volume. Hixson crowell equation is

$$Wo1/3 - Wt1/3 = Ks*t$$

Where, Wo= initial amount of drug in pharmaceutical dosage form
Wt= remaining amount of drug in pharmaceutical dosage form at time t
Ks= constant incorporating the surface volume relation
The data obtained are plotted as (percent drug release)1/3 verses time.

Korsmeyer-Peppas model:

To find out the mechanism of drug release, drug release data were fitted in Korsmeyer-Peppas equation which is expressed as:

$$Q/Q_0 = k\, t^n$$

Where, K_0 to K_2 were release rate constants
Q/Q_0 was fraction of drug released at time t,

K was constant and n was diffusion constant that indicates general operating release mechanism. For Fickian (diffusion controlled) n ≤0.5; for non Fickian (anomalous/zero order) release 'n' value is in between 0.5 to 1.0; for zero order release n=1.0; for super case transport II, n >1.0.

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as log cumulative percentage drug release *versus* log time

H) Fourier transform infrared spectroscopy (FTIR):

The samples were crushed with KBr to make pellets under hydraulic pressure of 600 kg, and then the FTIR spectra were recorded between 400 and 4000 cm-1.

I) Differential scanning calorimetric analysis (DSC):

The sample were heated from 0-3000C at heating rate of 100C/min underARGON atmosphere using a micrometer (DSC Q20 V24.4 Build 116, TAInstruments, USA) and then thermograms were obtained.

3. Results and Discussion

Compatibility Studies

Drug lipid compatibility studies were carried out using FTIR spectral studies to establish the possible interaction in the formulations. The IR spectrum of Venlafaxine, sodium alginate, pectin & gelatine their physical mixture is shown in Fig 2-5.

The IR spectrum of venlafaxine drug was compared with IR spectrum of physical mixture of drug and polymer. The presence of all characteristic peaks of Venlafaxine in the IR spectrum of drug-polymer mixture confirmed the absence of any chemical interaction between the two drugs and polymer. The results were shown in table 2.

Compatibility studies

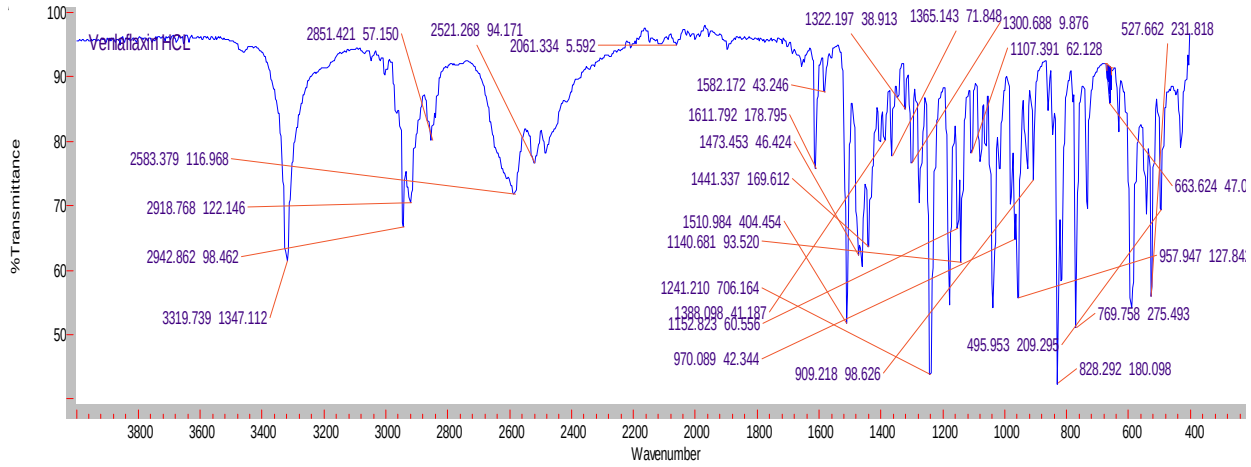

Fig .2 FT IR spectrum of pure drug venlafaxine hydrochloride

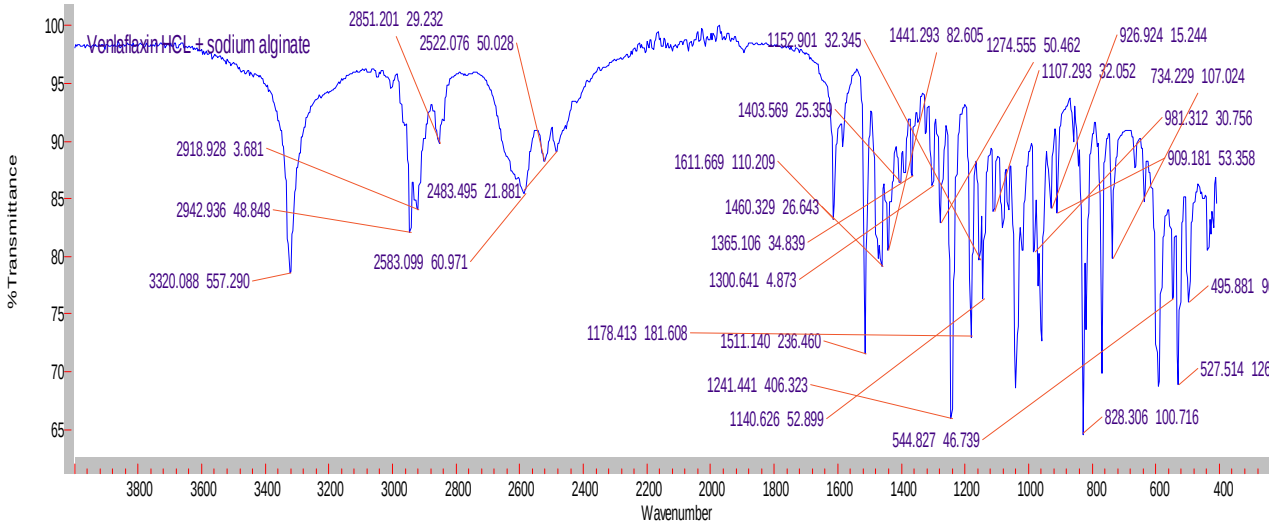

Fig.3 FT IR spectrum of pure drug venlafaxine hcl and sodium alginate

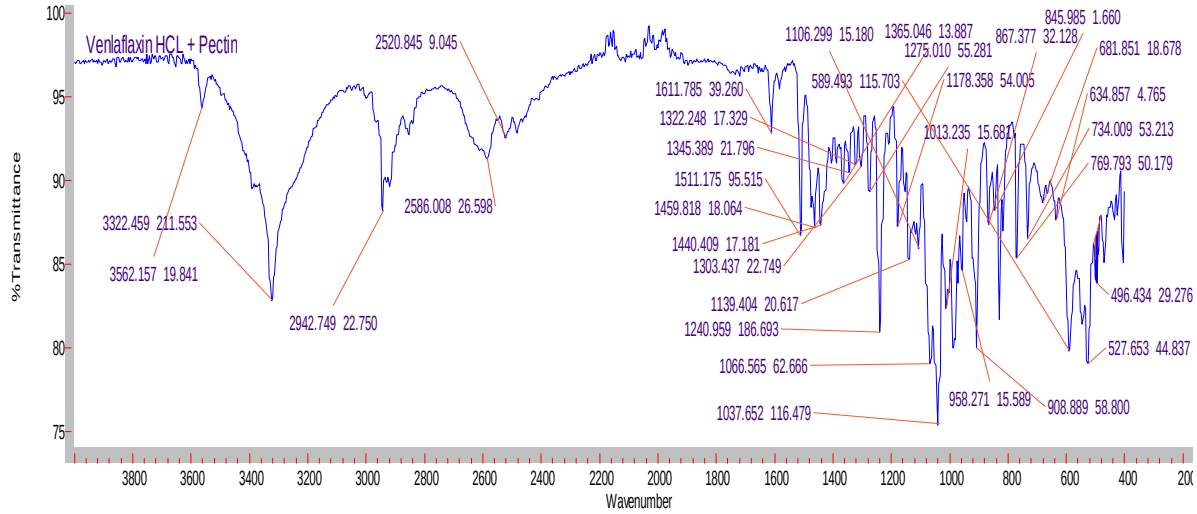

Fig.4 FT IR spectrum of Venlafaxine HCL and pectin

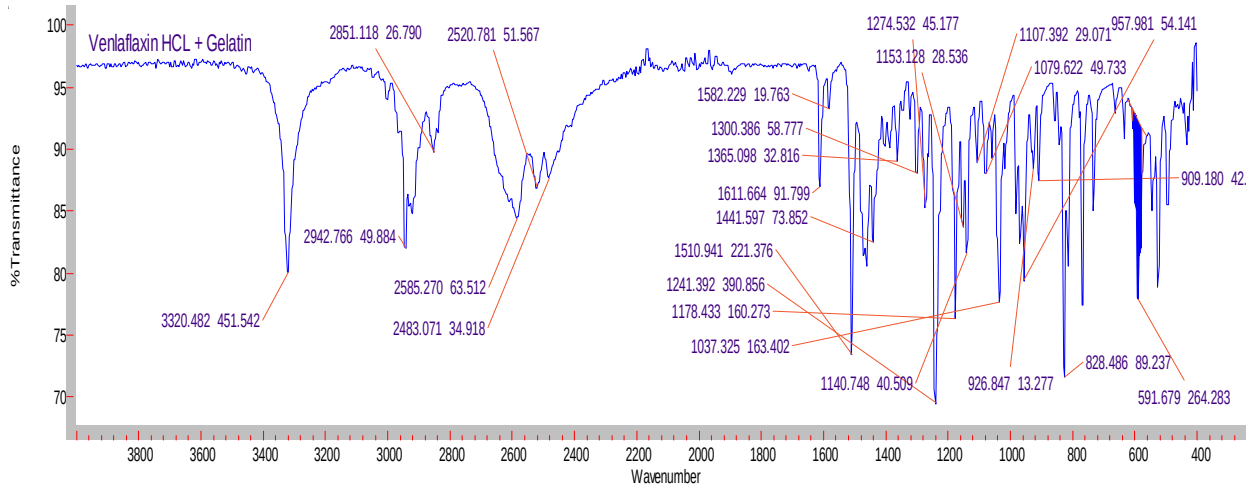

Fig.5 FT IR spectrum of Venlafaxine HCl and gelatin

Table 2 FTIR Spectral data of Venlafaxine HCL with Excipients

Functional group	Standard wavelength	Venlafaxine Hcl (Pure drug)	Venlafaxine Hcl +sodium alginate	Venlafaxine Hcl +gelatin	Venlafaxine Hcl+ pectin
-OH	3300-3650	3320	3320	3320	3562
C-C	500	495	497	502	496
C-OH	2500-3100	2942	2942	2943	2942
C-O	1030-1230	1140	1141	1179	1139

The FTIR spectrum of venlafaxine hydrochloride developed formulation revealead that major frequencies of functional groups of pure drug remain intact in the mixture of Venlafaxine HCL with different polymers . Hence there is no interaction between the drug and polymer used in the study

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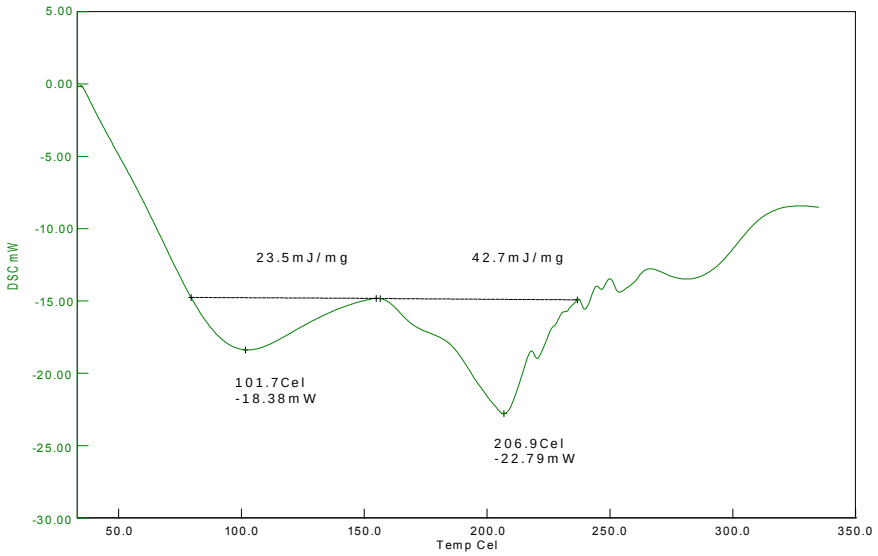

Fig.6 DSC Spectrum of venlafaxine hydrochloride, sodium alginate and pectin

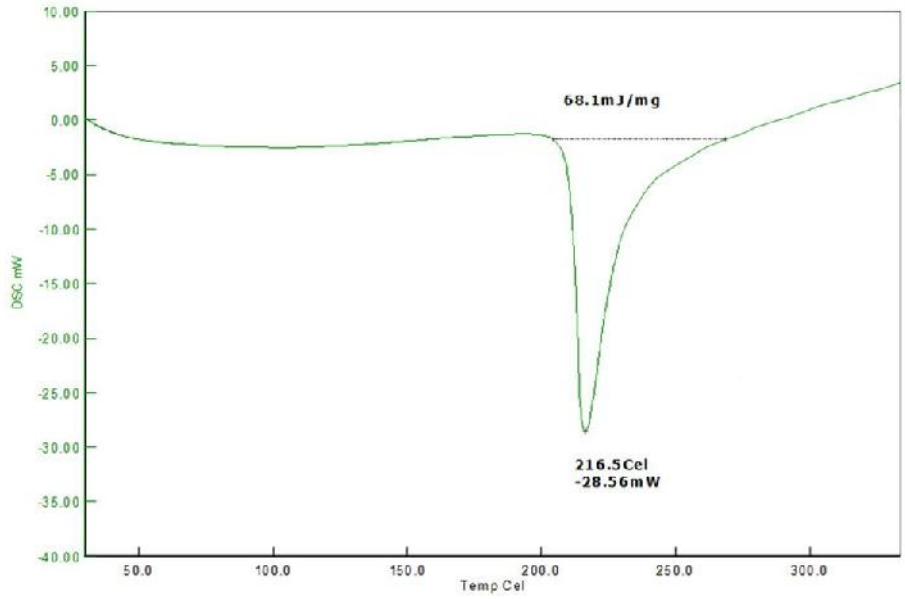

Fig.7 DSC Spectrum of Venlafaxine hydrochloride

Preparation of standard graphs

Standard graph of venlafaxine hydrochloride in 1.2 pH HCl

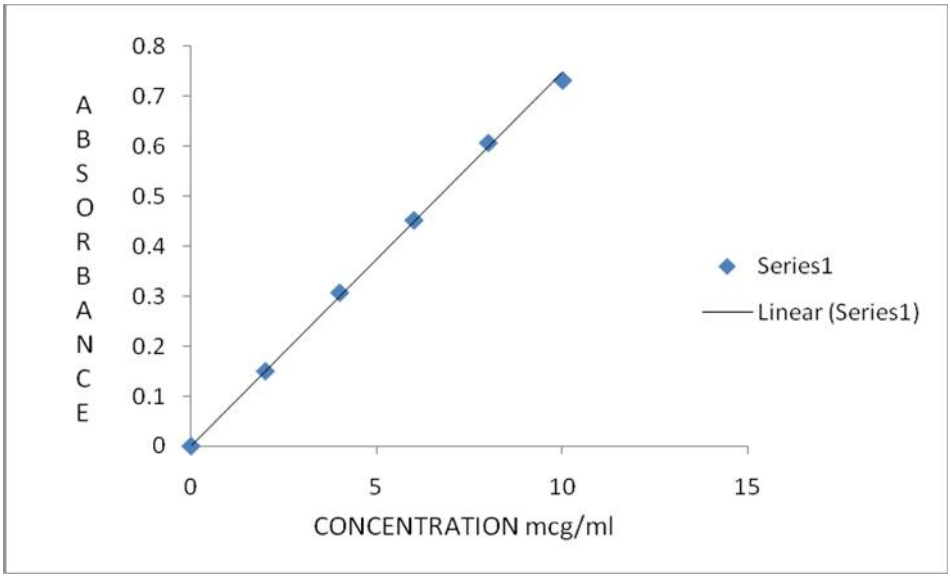

Fig.8 Standard curve of Venlafaxine hydrochloride in pH 1.2 Hcl buffer

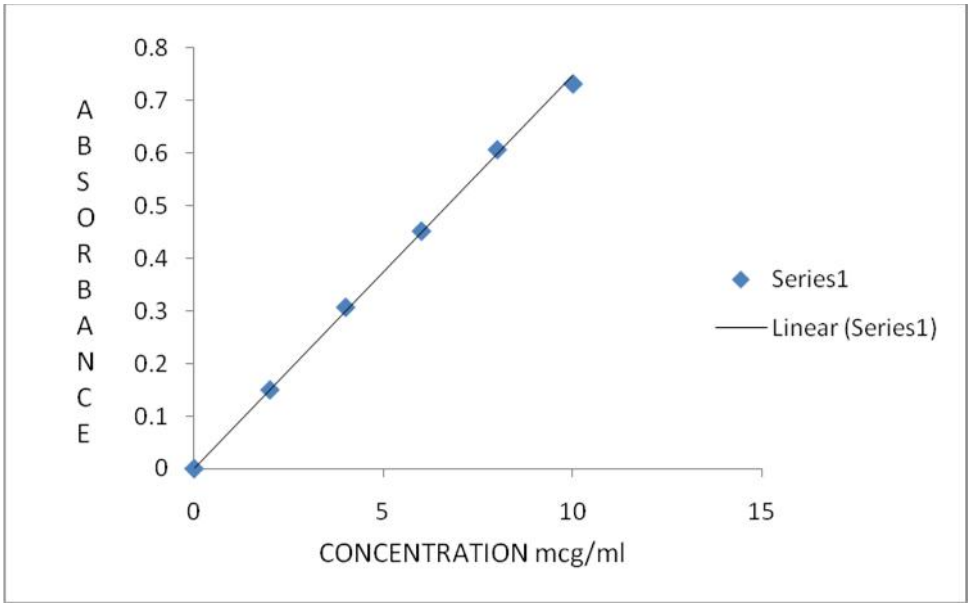

Fig.9 Standard curve of Venlafaxine in phosphate buffer pH 7.4

4.5 Particle size distribution

Table 3 Particle size distribution

Formulation	Particle size (µm) ±SD
F1	172±1.6
F2	185.4±0.8
F3	197.6±1.2
F4	160±1.4
F5	182±1.0
F6	**210.4**±1.8

The size of the beads was determined using optical microscope and recorded in table 3. The average bead size was found to be in the range of 172±1.6 to 210.4±1.8µm. By increasing the sodium alginate concentrations in the beads, an increase in size of the beads was observed, also, by increasing the amount of drug, an increase in size of the beads was observed.

Scanning Electron Microscopy:

They were found to be smooth surfaced spherical intact beads in the optimized formula (F6).

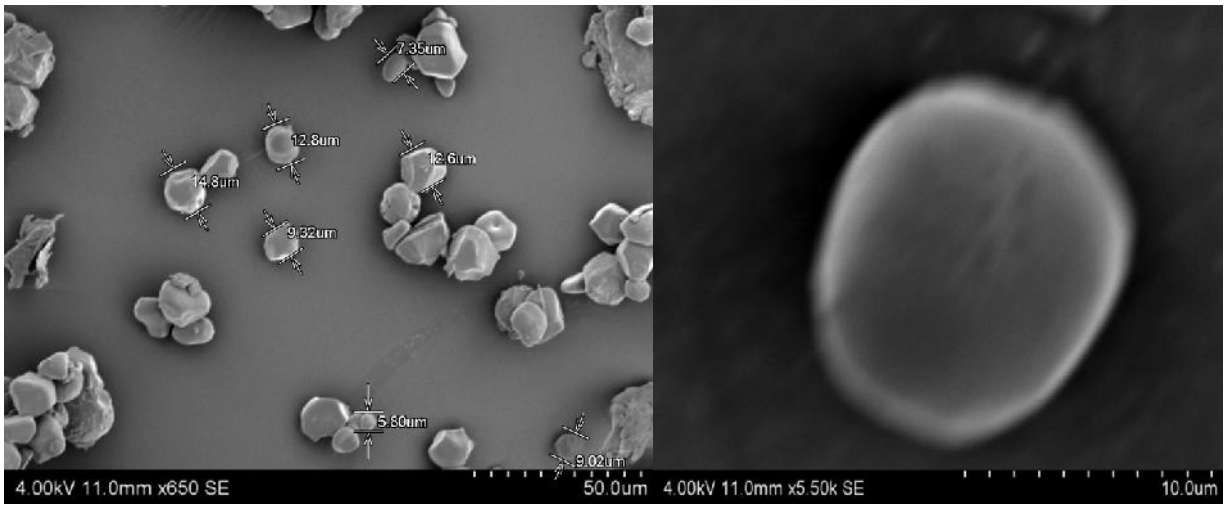

Fig.10 Scanning Electron Microscopic studies(F6)

4.5 Percentage yield and drug entrapment efficiency (dee) of venlafaxine microbeads

Percentage yield was found to be in range of 65% to85% . Maximum percentage yield was found to be 85% for F6 formulation. Percentage yield increases with increase in concentration of the polymer added to formulation.The drug entrapment efficiency (DEE) of the prepared microbeads was studied, and the results are given in table 4.The drug entrapment efficiency was found to be in the range of 60- 80 %.

Table 4 Percentage Yield and Drug Entrapment Efficiency (DEE) of venlafaxine Hydrochloride beads for various combinations. (F1- F6)

Formulation	Percentage yield	Drug entrapment efficiency(%)
F1	74.6±0.8	60±1.2
F2	57.3±1.0	68±1.4
F3	65.3±0.6	76±1.0
F4	77.6±0.8	69±0.6
F5	74.6±1.6	73±0.8
F6	**85**±1.2	**80**±1.4

The swelling study of microbeads in phosphate buffer pH 7.4

The swelling study of the prepared microbeads was carried out in phosphate buffer pH 7.4 and It was expressed as the ratio of initial weight of beads to the final weight of swollen beads as a function of time. The swelling of microbeads depends upon the concentrations of sodium alginate in the beads which increased with an increasing amount of sodium alginate in the beads.

Table 5 Swelling Index of F1 to F6 in Phosphate buffer pH 7.4

TIME (Hrs)	F1	F2	F3	F4	F5	F6
30	31	43	57	31	45	**66**
1	37	47	60	32	49	**69**
1.5	43	49	63	49	55	**72**
2	47	55	70	52	60	**80**
2.5	55	60	82	58	72	**85**
3	57	70	90	60	81	**97**

Table 6 *In vitro* cumulative %drug release data of Venlafaxine hydrochloride and gelatin microbeads

TIME (Hrs)	F1(%)	F2(%)	F3(%)
30	2±0.66	2±0.04	6±1.02
1	5±0.64	5±1.24	13±1.25
2	10±1.2	11±0.92	23±0.96
3	26±1.4	29±0.98	39±0.92
4	30±0.82	37±1.0	49±1.32
5	31±0.96	42±0.42	52±1.42
6	33±0.12	46±0.98	56±1.22
7	34±0.84	48±0.46	61±1.42
8	35±0.96	50±1.80	67±0.86
9	36±1.0	51±1.42	68±1.64
10	36±0.90	53±0.98	73±1.02

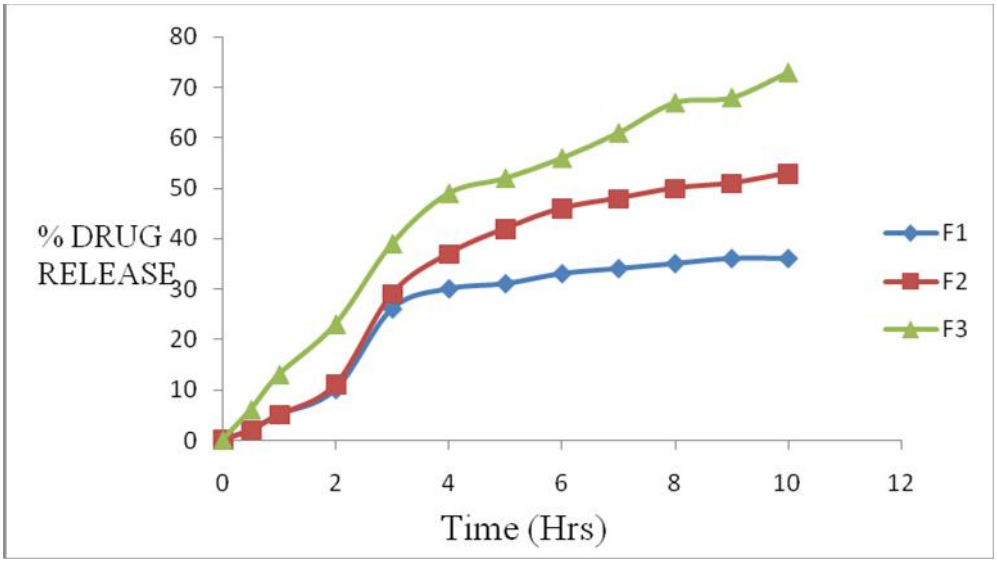

Fig.11 *In vitro* drug release profile of venlafaxine hydrochloride gelatin beads

Table 7 *In vitro* cumulative %drug release data of Venlafaxine hydrochloride pectin microbeads

TIME (Hrs)	F4(%)	F5(%)	F6(%)
30	6±1.2	6±1.4	23±0.82
1	13±1.0	13±0.92	37±0.96
2	25±0.8	25±0.84	41±0.48
3	28±0.6	39±0.68	56±0.86
4	39±0.6	49±0.72	63±0.94
5	49±1.0	52±0.93	69±1.4
6	52±0.9	56±0.58	77±1.6
7	56±0.8	61±0.74	86±1.2
8	58±0.4	67±0.92	89±0.84
9	60±0.8	68±1.02	90±0.92
10	61±1.0	75±1.04	92±0.94

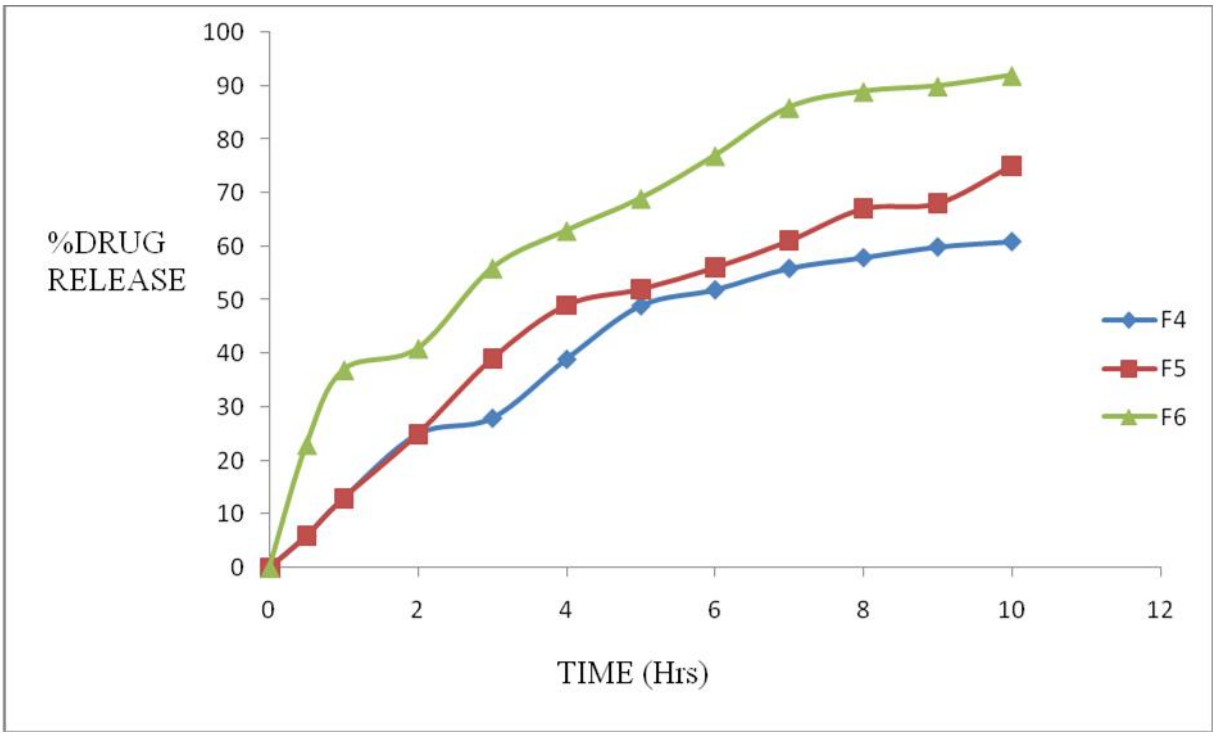

Fig.12 *In vitro* drug release profile of Venlafaxine hydrochloride pectin beads

The *in-vitro* drug release study was performed using dissolution test apparatus in phosphate buffer pH 7.4 and 0.1N Hcl.

The *in-vitro* drug release studies of gelatine microbeads (F1 to F3) the cumulative percentage drug release was observed in the range of 36 ±0.9% to 73±1.02%. The in-vitro drug release studies of pectin microbeads (F4 to F6) the cumulative percentage drug release was observed in the range of 61±1.0% to 92±0.94%. Compared to the gelatin microbeads pectin microbeads shows more sustained release. The best formulation was observed as F6.

4.8 Data analysis (curve fitting analysis):

For analyzing the mechanism of the drug release kinetics of the dosage form, the data obtained were fitted to various kinetic equations of zero order, first order, Higuchi model, hixson-crowell and Korsmeyer-Peppas model. The regression coefficient is calculated. Graphs of kinetic models were plotted with suitable data which was summarized in table no 4.10 . For first order release kinetics, for Higuchi release kinetics,for Hixson-crowell and for Korsmeyer-Peppas release kinetics.

Table 8 Kinetic data of optimized formulation F6

TIME	ROOT (T)	LOG (T)	CUMUATIVE %DR	LOG %DR	LOG %REMAIN	(%DR)1/3
0	0	-	0	-	2.000	0.000
0.5	0.707	0.301	23	1.362	1.886	0.387
1	1.000	0.000	37	1.568	1.799	0.663
2	1.414	0.301	41	1.613	1.771	0.749
3	1.732	0.477	56	1.748	1.643	1.111
4	2.000	0.602	63	1.799	1.568	1.309
5	2.236	0.699	69	1.839	1.491	1.500
6	2.449	0.778	77	1.886	1.362	1.798
7	2.646	0.845	86	1.934	1.146	2.231
8	2.828	0.903	89	1.949	1.041	2.418
9	3.000	0.954	90	1.954	1.000	2.487
10	3.162	1.000	92	1.964	0.903	2.487

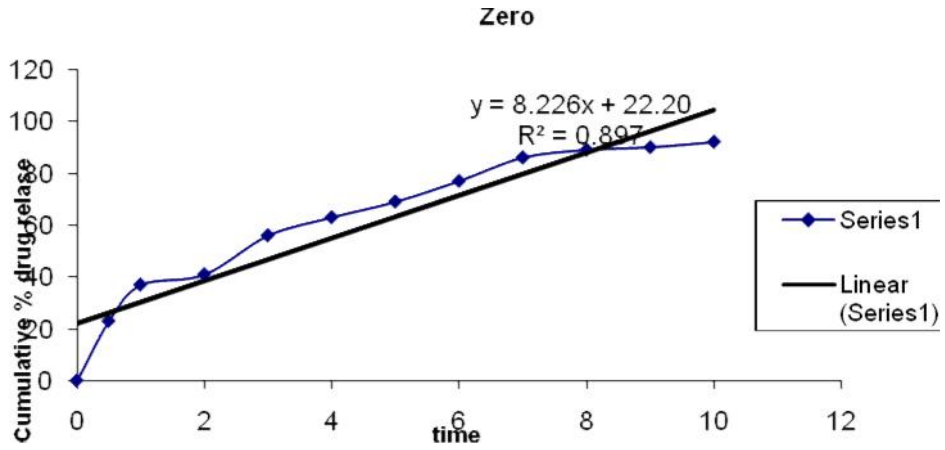

Fig.13 zeroorder release kinetics of optimized formulation F6

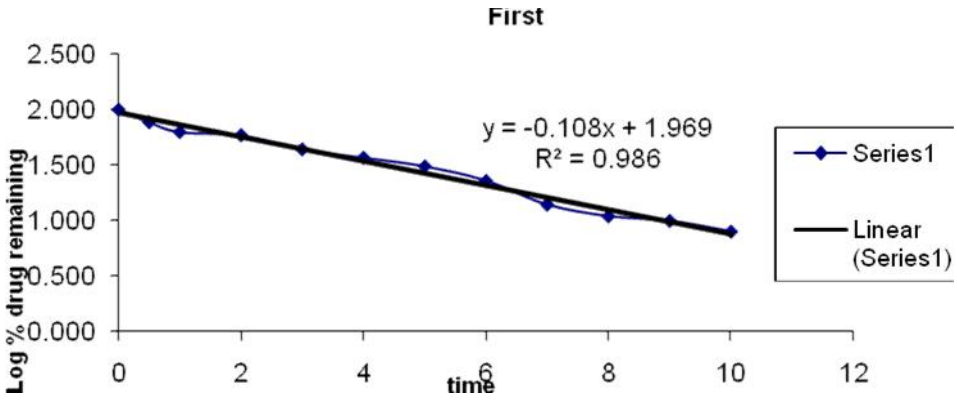

Fig.14 first order release kinetics of optimized formulation F6

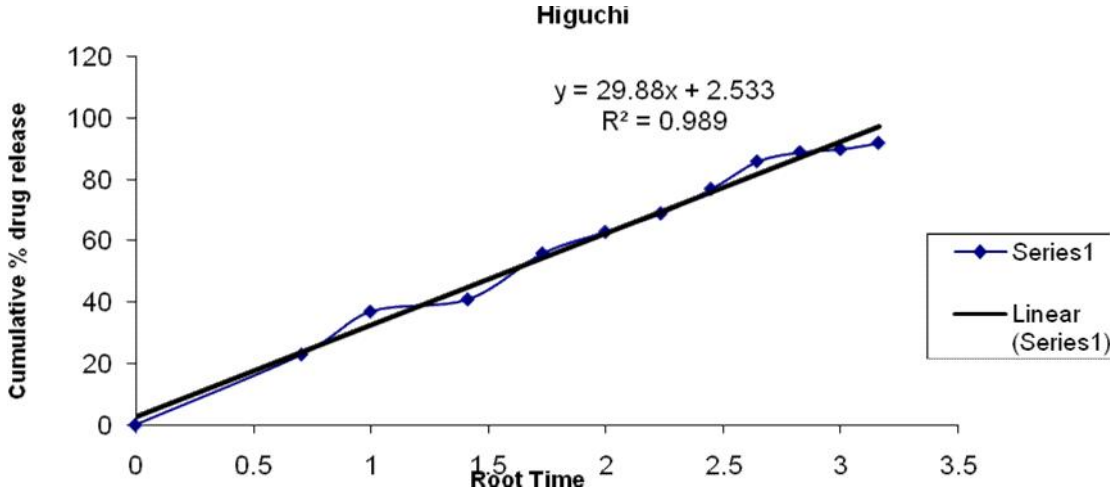

Fig.15 Higuchi release kinetics of optimized formulation F6

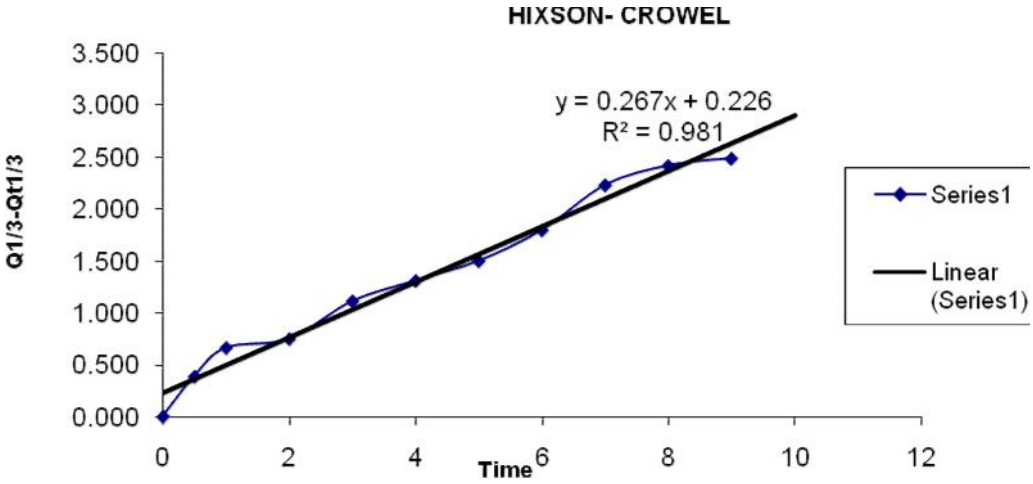

Fig.16 hixson crowell release kinetics of optimized formulation F6

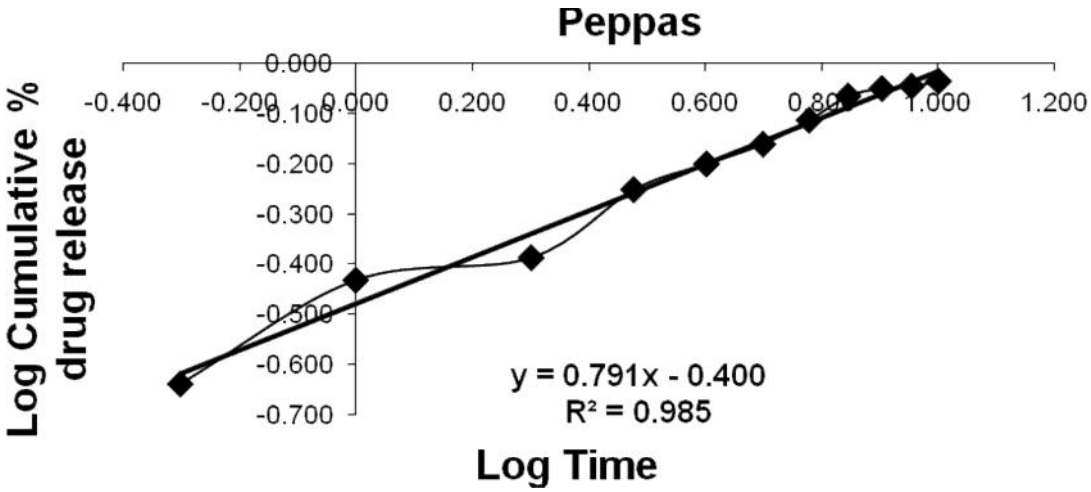

Fig.17 korsemeyer peppas release kinetics of optimized formulation F6

r^2 values of different kinetic models of microbeads

Table 9 r^2 values of different kinetic models

Formulation	Zero order	First order	Higuchi model	Korsemeyer peppas model		Hixson crowell model
				r^2	N	
F1	0.827	0.850	0.911	0.985	1.195	0.867
F2	0.898	0.934	0.935	0.985	1.332	0.935
F3	0.931	0.985	0.975	0.985	0.923	0.970
F4	0.923	0.964	0.973	0.985	0.855	0.967
F5	0.935	0.987	0.978	0.985	0.921	0.970
F6	0.897	0.986	0.989	0.985	0.463	0.981

Where, r^2 = regression coefficient
n = slope

Based on the mathematical data revealed from kinetic models, it was concluded that the release data was best fitted with Higuchi model. Higuchi equation explains the diffusion controlled release mechanism, the diffusion exponent 'n' values were found to be less than 0.5 indicating Fickian diffusion.

Conclusion

Sodium alginate- pectin based microbeads comprising of venlafaxine hydrochloride can be successfully formulated by ionotropic gellation method. The preformulation studies like melting point, solubility and UV analysis of venlafaxine hydrochloride complied with IP standard. Compatibility studies are carried out by FT-IR spectroscopic studies revealed that there is no significant interaction between drug and polymer. Polymer- drug ratio showed an influence on the particle size, swelling index, cumulative % drug release and drug entrapment efficiency. Among the six batches F6 showed better drug release of 92±0.94% for 10hrs which is matchingthe objective of the study. Therefore, it is concluded that the venlafaxine hydrochloride microbeads prepared with sodium alginate and pectin inthe ratio of 3:1 is a successful pharmaceutical dosage form for providing sustained release drug delivery of the drug and improving bioavailability.

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