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FORMULATION AND *IN-VITRO* EVALUATION OF GASTRO RETENTIVE FLOATING TABLET OF VENLAFAXINE HYDROCHLORIDE BY HOT-MELT EXTRUSION METHOD

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Keywords:

Gastro Retentive, Venlafaxine hydrochloride, hot melt extrusion, Guar gum, Xanthan gum, HPMC K15M

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ABSTRACT: Drugs that have a proximal absorption window can be improved by the Gastro Retentive Drug Delivery System which provides continuously releasing the drug for a prolonged period of time as controlled delivery before it reaches its absorption site, thus ensuring its optimal bioavailability. The intend of this current work is to formulate a gastro retentive floating tablet of Venlafaxine hydrochloride by hot-melt extrusion method. The buoyancy of tablet leftovers for 24 hours in the stomach and in a controlled way the drug was released. In the present work, by using the direct compression method, various formulations were made, in which HPMC K15M, Guar gum, and Xanthan gum were included as swelling polymers, sodium bicarbonate as gas generating agent, and MCC as diluent, talc, and magnesium stearate used as glidant &lubricant respectively. By the UV spectroscopic and IR spectroscopic interpretation, the characterization of the drug was recognized. The hardness, friability, uniformity of weight, drug-polymer interaction, *in-vitro* floating studies, Swelling Index & *in-vitro* drug release studies were evaluated for all the prepared floating formulations. It can be concluded from the results that floating lag time decreased as the concentration of the polymer increased and the percentage drug release was extended. The viscosity of the polymer also showed a directly proportional relationship with the swelling characteristics of the tablets.

INTRODUCTION: More predictable and improved bioavailability of drugs should be mainly intended to accomplish by the oral controlled drug delivery systems (CDDS). However, several physiological difficulties is unacceptable during the development process, includes the highly variable nature of the gastric emptying process and an inability to hold down and localize the CDDS within the desired gastrointestinal (GI) regions.

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It can be imagined that the emptying process can last from a few minutes to 12 h depending upon the physiological state of the subject and the design of pharmaceutical formulation. Since the majority of drugs are preferentially absorbed in the upper part of the small intestine, this inconsistency, in turn, however, may show the way to unpredictable bioavailability and time to reach peak plasma levels.

Moreover, incomplete drug release from the CDDS leading to diminished efficacy of the administered dose results from the relatively short gastric emptying time (GET) in humans, which normally averages 2-3 h through the major absorption zone (stomach or upper part of the intestine). These considerations have to lead to gastric retaining oral

controlled-release (CR) dosage forms. Prolonged gastric retention is useful for drugs acting locally in the Gastric region, poorly soluble and unstable in intestinal region and also gets better bioavailability, diminishes drug waste. Recently, a range of efforts are being ended to create gastro retentive systems such as floating, swelling and expanding, bioadhesive/mucoadhesive, modified shape, low density/high density and raft systems *etc*.

Due to exact site absorption limitations, these systems are beneficial in getting better GIT absorption of drugs with CR. Gastric floating drug delivery systems (GFDDS) offer numerous advantages over the gastric retentive systems among the various gastro retentive systems. These systems remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time since it has a density lower than the gastric fluids.

The drug is released slowly at a desired rate from the stomach, while the system is floating on the gastric contents [1, 2]. An extremely efficient anti-depressant, Venlafaxine HCl, was opted as a model drug to extend a controlled release formulation. Venlafaxine HCl exhibits pH-reliant solubility. The solubility of drug in acidic pH was more and at neutral or alkaline condition (intestinal environment) was insignificant. Hence an effort was made to develop gastro retentive delivery system of Venlafaxine HCl, which reduced frequency of administration, thereby improving patient compliance and therapeutic value and also enhanced the bioavailability of Venlafaxine HCl_3, [4].

METHOD:

Pre formulation Studies [5]: Pre formulation testing is the initial juncture in the rational progress of dosage form. The physical and chemical properties of drug substances independently and collectively with pharmaceutical excipients were investigated.

Compatibility Studies: The KBr pellet method was involved in the drug-excipients interaction study. The solid admixtures were equipped by blending the drug with each formulation excipients individually in the ratio of 1:1, and it was packed and characterized by using Fourier transform infrared spectroscopy (FT-IR) to spot the compatibility of various formulation excipients with Venlafaxine HCl.

UV- Spectrum Analysis of Drug: Using UV-Spectrophotometer, drug solution was prepared to pH 1.2 with 0.1N HCl and examined the solution between the range 220-380 nm and the maximum wavelength of the drug was established at 224nm.

Standard Curve of Venlafaxine Hcl: According to the Beer's –Lambert's law limit ranging 2-20 µg/ml, Venlafaxine Hcl can be estimated spectro metrically at 224 nm. A stock solution of 1000 µg/ml concentration is prepared by dissolving 100 mg of Venlafaxine Hcl in 100 ml of 0.1N HCl. Further concentration of 100 µg/ml solution is made by diluting 10 ml of stock solution to 100 ml of 0.1N HCl.

In 10 ml volumetric flask, 0.2 ml to 1ml of standard drug solution was transferred and diluted with 0.1N HCl up to the mark to attain the final concentration ranges from 2-10 µg/ml. With0.1N HCl as a blank, Absorbance of each solution was measured at 224 nm. A plot was drawn between concentrations of drug vs. absorbance.

Preparation of Venlafaxine HCl Floating Tablets: Hot Melt Extrusion (HME) method is employed in the preparation of tablets. The compositions of the formulations were shown in **Table 1**. In this process, the polymeric carrier embeds the drug. Exclusively, Drug, functional Excipients, and processing aids are blended uniformly to form a complex mixture in the case of HME dosage forms. In the china dish, the calculated amount of Beeswax was melted. Blend of polymers, diluents followed by the active pharmaceutical ingredient are added geometrically in molten mass [6, 7, 8, 9, 10].

Blend well to avoid solidification before mixing and later cooled to room temperature to obtain coherent mass which was scrapped from the hot plate and passed through sieve no 36 to form granules. The fine granules were removed by passing again through sieve no 100. Finally, the formed granules admixed with calculated amount of glidant and lubricants are compressed using rotary tablet punching machine.

TABLE 1: COMPOSITION OF VENLAFAXINE HCL FLOATING TABLETS

Ingredients	F01 (mg)	F02 (mg)	F03 (mg)	F04 (mg)	F05 (mg)	F06 (mg)	F07 (mg)	F08 (mg)	F09 (mg)
Venlafaxine Hcl	75.0	75.0	75.0	75.0	75.0	75.0	75.0	75.0	75.0
Guar gum	45.0	75.0	90.0	_	_	_	_	_	_
Xanthan gum	_	_	_	45.0	75.0	90.0	_	_	_
HPMC K15M	_	_	_	_	_	_	45.0	75.0	90.0
Bees wax	45.0	45.0	45.0	45.0	45.0	45.0	45.0	45.0	45.0
MCC	75.0	55.0	30.0	75.0	55.0	30.0	75.0	55.0	30.0
Sodium bicarbonate	45.0	45.0	45.0	45.0	45.0	45.0	45.0	45.0	45.0
Magnesium stearate	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Talc	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
Total	300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0

Evaluation Parameters: [11, 12, 13, 14, 15]

Micromeritic Properties of Granules:

Bulk Density: Bulk density is the ratio of powder weight to that of the bulk volume of the powder. Shape and cohesiveness of particles and Particle size distribution influence the bulk density property of the powder. A graduated measuring cylinder was taken in which precisely weighed mass of powder was carefully poured, and volume was measured which waster med as initial bulk volume. With the value of mass of powder and initial bulk volume, Bulk density is calculated and expressed in gm/cc.

Tapped Density: A spotless, dried-out 100 ml measuring cylinder was filled with ten gms of powder. Tapped volume was read after 100 tapping of the cylinder from an even height. With the value of mass of powder and tapped volume, Tapped density is calculated and expressed in gm/cc.

Angle of Repose (Θ): At a given height (h) a funnel was fixed with its tilt, under which a graph paper was positioned on plane surface. Through the funnel till the tip of the conical pile just touches the tilt, the powder was cautiously transferred. On measuring the height and radius of the heap, the angle of repose was intended.

Carr's Compressibility Index: Carr urbanized atortuous method of measuring powder flow from bulk densities. The direct measurement of the potential powder arch or the bridge strength and stability confers the percentage compressibility of powder. Carr's compressibility index was calculated for each formulation.

Physico Chemical Characterization of Tablets:

Thickness: Consumer acceptance and tablet uniformity depends on the physical dimension of the tablet, such as thickness. Using Vernier calipers, the thickness and diameter of the tablet was measured. It is represented in mm.

Hardness: While handling the tablets, the ability to withstand mechanical shocks is indicated by their Hardness. To establish the tablet mechanical strength, Monsanto hardness tester was used. Between an immovable and moving jaw, the tablet was seized. The load was progressively raised after the scale was adjusted to zero and continued until the tablet splintered. The value of the load at that point offers a measure of the hardness of the tablet. Randomly picked 3 tablets were utilized to determine the hardness of the tablets and expressed in Kg/cm^{-2}.

Friability: Roche Friabilator was used in testing the Tablet strength. In the friabilator 20 pre-weighed tablets are placed and taken out after 100 revolutions (4 min) and dedusted. By reweighing the tablets, the percentage of weight loss was calculated. The % friability was then calculated.

Weight Variation: Randomly selected 10 tablets from each batch were weighed individually and together in a single pan balance. The standard deviation was calculated after noting the average weight. If not more than two tablets fall outside the percentage limit and none of the tablets differs by more than double the percentage limit, then the tablet passes the test.

Swelling Index: To expand the insight on the observed trend of drug release with the rates of polymer hydration, the measurement of the swelling rate of the floating matrix tablet was carried out. By using USP dissolution apparatus-II in 900 ml of 0.1N HCl, which is maintained at 37 ± 0.5 °C, rotated at 50 rpm, swelling index of the dosage form is conducted. The tablet was

withdrawn at selected regular intervals and the surplus water was stained with tissue paper and the swelling index was calculated.

Buoyancy Studies: Floating lag time was determined to assess the *in-vitro* floating behavior (buoyancy) of the tablets. In 100 ml beaker containing 0.1 N HCl (pH 1.2), the tablets were placed. The floating lag time (time taken by the tablet to arrive at the surface) and total floating time (floating period of the tablet) were resolved.

***In-vitro* Release Studies:** USP dissolution apparatus II was used to determine the drug release rate. 900 ml of simulated gastric fluid (pH 1.2) maintained at 37 ± 0.1 °C was selected as the dissolution media and stirred at 50 rpm. By compensating with fresh dissolution medium, the samples were introverted at appropriate time intervals and assayed spectro photometrically at 224 nm in Shimadzu U.V. spectrophotometer. Samples were assayed in triplicate.

Kinetic Analysis of *In-vitro* Drug Release Rates: So as to pick up the knowledge into the drug release mechanism, the release data were analyzed for best fitting into zero-order, first-order, and Higuchi's square root of time mathematical models, the Hixson and Crowell powder dissolution method and the Korsmeyer and Peppas model.

RESULTS:

Standard Curve of Venlafaxine HCl:

TABLE 2: STANDARD CURVE OF VENLAFAXINE HCl

S. no	Concentration (µg/ml)	Absorbance at 224nm
1	0	0
2	2	0.144
3	4	0.303
4	6	0.479
5	8	0.655
6	10	0.768

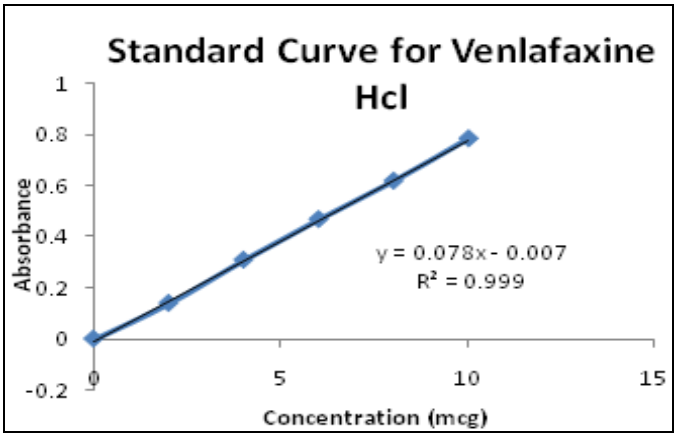

FIG. 1: STANDARD CURVE OF VENLAFAXINE HCL

FTIR Studies:

TABLE 3: COMPATIBILITY STUDIES OF VENLAFAXINE HCL WITH EXCIPIENTS

S. no	Excipients	60% ± 5% RH /35 ˚C ± 2⁰C (3 weeks)	Excipients / Drug ratio	Initial Physical description
1	Venlafaxine HCl	#	-	Crystalline white powder
2	Drug + HPMC k15M	#	1:1	Crystalline white powder
3	Drug + Xanthan gum	#	1:1	Crystalline white powder
4	Drug + Guar gum	#	1:1	Crystalline white powder

# indicates nil incompatibility

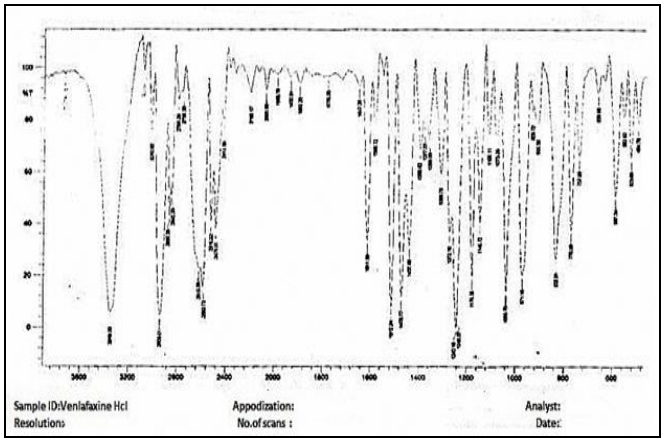

FIG. 2: FTIR SPECTRUM OF API

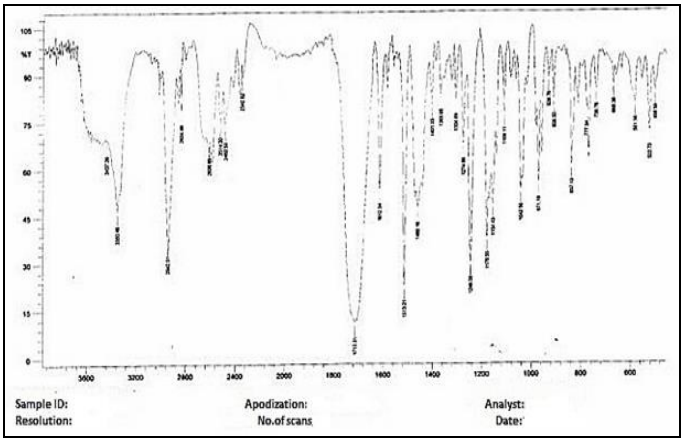

FIG. 3: FTIR SPECTRUM OF API+ GUAR GUM

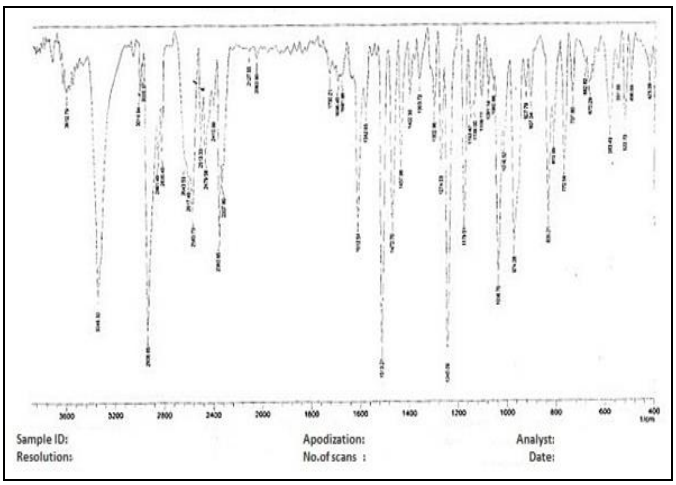

FIG 4: FTIRSPECTRUM OF API+ XANTHAN GUM

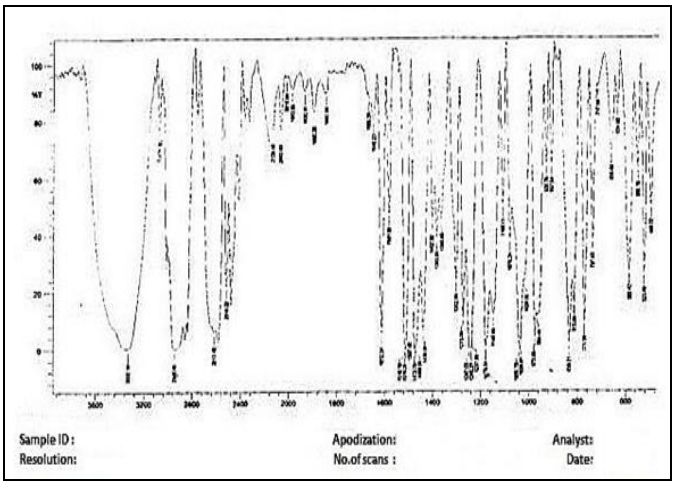

FIG 5: FTIR SPECTRUM OF API+ HPMC K15M

TABLE 4: INTERPRETATION DATA OF IR SPECTRA OF VENLAFAXINE HCl FOR COMPATIBILITY STUDIES

S. no	Vibrations types	Absorption Ranges(cm^{-1})	Drug (cm^{-1})	Physical mixture of drug + polymer		
				Drug + Xanthan gum	Drug + guar gum	Drug + HPMC K15M
1	Aromatic C=C stretching	1680-1600	1642.8	1638.8	1634.2	1640.7
2	Aromatic C-H stretching	3000-2850	2942.1	2939.1	2948.4	2934.0
3	C-O stretching	1300-1000	1239.1	1251.2	1235.8	1233.6
4	O-H stretching	3400-3600	3352.2	3343.8	3446.1	3338.9
5	C-N stretching	1350-1000	1310.4	1307.4	1303.4	1311.4
6	N-H stretching (1˚ & 2˚amine)	3500-3100	3351.8	3341.3	3456.4	3349.5

Evaluation Parameters:

Micromeritic Properties of Granules:

TABLE 5: MICROMERITIC PROPERTIES OF GRANULES

Formulation	Angle of repose	Bulk Density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)
F01	27·5	0.335	0.465	18.654
F02	28.6	0.312	0.445	20.731
F03	31. 5	0.324	0.435	19.144
F04	29 .4	0.350	0.446	18.361
F05	31. 7	0.348	0.483	20.477
F06	32. 8	0.395	0.434	19.641
F07	29.3	0.346	0.442	17.493
F08	30·6	0.303	0.495	18.954
F09	28.0	0.314	0.415	19.745

Physico Chemical Characterization of Floating Tablets

TABLE 6: POST COMPRESSION PARAMETERS OF FLOATING TABLETS

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Average weight variation(mg)	Drug content
F01	3.53	5.55	0.22	300.6	98.66
F02	3.96	5.52	0.51	301.1	99.61
F03	3.25	5.89	0.84	300.6	97.86
F04	3.65	5.86	0.52	299.9	99.64
F05	3.52	5.45	0.64	298.4	98.10
F06	3.86	5.65	0.42	300.6	97.89
F07	3.96	5.69	0.61	299.4	99.66
F08	3.49	5.20	0.57	299.6	97.61
F09	3.78	5.62	0.48	300.6	98.53

Swelling Index:

TABLE 7: SWELLING INDEX (%) OF FLOATING TABLETS

Time	Formulations								
	F01	**F02**	**F03**	**F04**	**F05**	**F06**	**F07**	**F08**	**F09**
1	46.6	41.5	38.5	41.6	38.5	34.9	24.9	18.4	15.6
2	79.2	72.9	70.6	72.5	73.9	69.6	35.4	37.6	33.4
3	125.2	109.9	107.9	112.4	108.4	106.4	70.6	68.6	57.7
4	138.5	141.4	134.1	141.9	135.9	128.6	115.4	99.4	87.4
5	156.8	162.4	159.4	164.5	163.1	158.7	125.3	110.4	109.1
6	168.6	172.9	168.9	172.8	168.6	164.9	136.4	124.4	119.9
7	174.8	178.4	176.6	181.1	174.4	171.2	138.6	132.2	128.4

In-vitro Drug Release Studies:

TABLE 8: PERCENTAGE DRUG RELEASE OF FORMULATIONS

Time (hrs)	FORMULATIONS								
	F01	**F02**	**F03**	**F04**	**F05**	**F06**	**F07**	**F08**	**F09**
1	19.45	21.68	19.47	22.16	26.48	26.10	27.24	29.14	27.15
2	33.48	32.19	29.75	31.47	40.15	36.48	42.95	38.49	36.48
3	43.84	41.97	39.48	44.18	51.49	43.94	50.49	46.28	42.81
4	54.18	50.18	49.75	50.43	56.19	50.04	58.12	56.49	51.21
5	60.14	58.41	54.66	60.57	61.57	54.87	65.99	63.48	59.45
6	66.54	63.55	61.43	69.77	66.32	63.14	70.15	69.11	64.58
7	75.16	72.19	69.47	70.15	71.89	67.21	79.41	76.46	68.16
8	81.54	78.25	76.34	78.95	76.64	71.24	84.69	78.41	73.33
9	86.15	82.22	80.41	84.77	78.45	79.66	87.14	84.95	80.78
10	88.95	84.18	83.54	87.15	84.22	83.96	94.74	89.36	84.26
11	91.98	88.25	84.87	90.48	88.96	86.56	99.24	94.28	90.44
12	95.21	91.24	89.34	95.68	94.22	92.58		99.45	94.86

Buoyancy Studies:

TABLE 9: BUOYANCY STUDIES OF FLOATING TABLETS

Formulation code	Floating lag time (sec)	Floating duration (hrs)
F01	28	>11
F02	34	>11
F03	35	>11
F04	30	>11
F05	31	>11
F06	32	>11
F07	27	>11
F08	26	>11
F09	34	>11

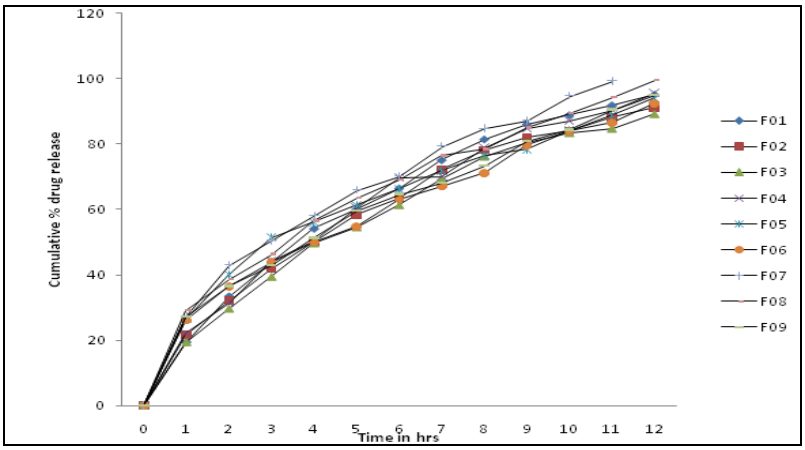

FIG. 6: *IN-VITRO* DISSOLUTION PROFILE OF F1 TO F9 FORMULATIONS

Release Kinetics:

TABLE 10: MODEL FITTING FOR FORMULATION F-8

Time (Hrs)	% Drug released	Log % released	Log t	Square root of time	Log cumulative % drug released
0	0	2	0	0	0
1	29.14	1.85	0	1	1.464
2	38.49	1.77	0.30	1.41	1.585
3	46.28	1.71	0.47	1.73	1.665
4	56.49	1.64	0.60	2	1.751
5	63.48	1.56	0.69	2.23	1.802
6	69.11	1.50	0.77	2.44	1.839
7	76.46	1.39	0.84	2.64	1.883
8	78.41	1.31	0.90	2.82	1.894
9	84.95	1.14	0.95	3	1.929
10	89.36	1.04	1	3.16	1.951
11	94.28	0.67	1.04	3.31	1.974
12	99.45	-0.09	1.07	3.46	1.997

TABLE 11: CORRELATION COEFFICIENTS OF DIFFERENT FORMULATIONS

Formulations	Zero Order value (R^2)	First Order value (R^2)	Higuchi Value (R^2)	Korsemeyer Peppa's		Hixson Crowell
				(R^2)	n-value	
F01	0.940	0.981	0.991	0.994	0.60	0.997
F02	0.938	0.993	0.992	0.994	0.60	0.995
F03	0.944	0.995	0.988	0.994	0.64	0.995
F04	0.941	0.975	0.994	0.997	0.59	0.996
F05	0.894	0.944	0.994	0.991	0.46	0.971
F06	0.942	0.970	0.997	0.993	0.51	0.990
F07	0.933	0.825	0.999	0.998	0.53	0.960
F08	0.929	0.821	0.999	0.998	0.49	0.957
F09	0.942	0.956	0.997	0.995	0.52	0.986

DISCUSSION: The gastric residence time of the drug was increased by developing Floating tablets of Venlafaxine HCl so that they can help in controlled release of drug up to 12 h by retaining in the stomach for an extended time. Different viscosity grades of guar gum, Xanthan gum, HPMC K15M polymers are advantageous in getting better buoyancy property and release characteristics.

Determination of λ_{max}: Using UV-spectro-photometer, drug solution was prepared to pH 1.2 with 0.1N HCl and examined the solution between the range 220-380 nm and the maximum wavelength of the drug was established at 224 nm and the results were shown in **Table 2**. According to the Venlafaxine HCl standard curve, it was observed that the drug obeys Beer's law in the range of 2-20 µg/ml.

Incompatibility Studies: FTIR spectra of pure drug (Venlafaxine HCl), Guar gum, HPMC K15M, Xanthan gum, and a mixture of drug with the above polymers were taken and compared in order to verify the compatibility of the drug in the formulation. The FTIR spectrum of Venlafaxine HCl reveals the presence of peaks at 2942.1 due to the presence of C-H stretching, 1642.8 due to the presence of C=C aromatic stretching, 3352.2 due to the presence of O-H stretching, 1239.1due to the presence of C-O stretching, 3351.8 due to the presence of N-H stretching, 1310.4 due to the presence of C-N stretching and the results were shown in **Table 3**, **4**. Major frequencies of functional groups of pure drug stay unblemished in a powder containing guar gum, HPMC K15M and Xanthan gum. Hence there is no major interaction between the drug and polymers used in the study.

Micromeritic Properties of Granules: The Micromeritic properties obtained for all formulations are tabulated in **Table 5**. The good flow property of the powder blend was observed since the angle of repose value was found to be in the range of 27.5 to 32. 8. Further required flow property for compression of powder blend is confirmed with Carr's index value which ranges between 17.493 to 20.731%.

Physicochemical Characterization of Floating Tablets: Using the polymers guar gum, Xanthan gum, HPMC K15M, the floating tablets were manufactured by direct compression method to supply satisfactory drug release retardation and give adequate buoyancy to the tablets. The results have shown in **Table 6**. The physicochemical characters of prepared floating tablets were evaluated for thickness, hardness, friability, average weight variation; all the studies were performed in triplicates, and the results were expressed. The good handling characteristics of all the batches were ensured by the measured hardness for the tablets, which arranged between 5.20 to 5.89 kg/cm^{-2}. Mechanical stability of all the formulations was made certain from the % friability of the tablets which was less than 1%.

The weight variation of all the formulations was seen to be 298.4 to 301.1, which demonstrates consistency in each batch. The swelling index for all the formulations was carried out in the 0.1N HCl as swelling media which showed different indices were shown in **Table 7**. Maximum swelling in 7 h was attained in tablets containing xanthan and guar gum. The tablets were placed in a beaker containing 0.1 N HCl (pH 1.2) and *in-vitro* floating behavior was studied. The dosage unit floated immediately, generating sufficient porosity because of the evolution of carbon dioxide from the gas-generating agents in the presence of HCl solution.

After 28 sec, Formulation F1-F3 prepared with guar gum started floating and remains buoyant for 11 hr till they were completely eroded. Formulation F4-F6 prepared with Xanthan gum, on the other hand, shows a floating time of 12hrs, and formulation F7-F9 prepared with HPMC K15M showed a decrease in floating lag time of 26 sec and increased floating duration to greater than 11 h. The integrity of the tablets for a longer duration by reducing the effect of erosion might be due to high viscosity polymer HPMC K15M thus resulting in increased floating time. The results are shown in **Table 8**.

Thus the batch containing HPMC polymers showed good floating lag time and total floating time. Using USP dissolution apparatus type II, *in-vitro* drug release studies were carried out. The dissolution medium consisted of 900 ml of pH 1.2 acid buffer (0.1N HCl), maintained at 37 ± 0.5 ºC at 50 rpm. At different time intervals, samples were measured for drug release using an ultraviolet, visible spectrophotometer at 224 nm. Formulations F1-F3 prepared with Guar gum showed drug release as 95.21, 91.24, and 89.34%, respectively, whereas formulation F4- F6 prepared with Xanthan gum was found to be 95.68, 94.22, and 92.58% at the end of 12 h. Formulation F7 prepared with HPMC K15M showed 99.24% at the end of 11 hours. However, formulations F8 and F9 prepared with increased concentrations of HPMC K15M showed 99.45 and 94.86% at the end of 12 hours. As per the results of the dissolution study, the formulations F01, F02, F03, F04, F05, F06, F08, F09 prolonged the drug release for 12 h. while F7 prolonged the drug release for 11 h. All the formulations were designed as a dosage form for 12 h. Formulations were subjected to dissolution studies for 12 h in order to check the 100% dissolution release profile.

Among the nine formulations, F8 was best and shows 99.45% drug release at the end of 12 h. It is obvious from the *in-vitro* dissolution data that an increase in HPMC K15M concentration decreases the release rate; this might be due to an increase in diffusion path length, which the drug molecule may have to pass through. So, formulation F8 was selected as the optimized formulation. The results are shown in **Table. 9**.

The *in-vitro* drug release data of the floating tablets were evaluated kinetically by zero-order kinetics, first-order kinetics, Higuchi kinetics, Korsemeyer Peppa's and Hixson-Crowell's kinetic models, and the results were depicted in **Table 10**. The regression coefficient (R^2) value for Zero order, First order, Higuchi's, Hixson Crowell's, and Peppa's plots of all formulations were depicted in **Table 11,** and optimized formulation F8 showed 0.929, 0.821, 0.998, 0.957, and 0.999, respectively. The optimized formulation F8 followed Higuchi's plot. The drug release depends on the square root of the time and is predominantly controlled by the diffusion process since the regression coefficient is 0.999, and also plots were found to be linear. The drug release mechanism is predicted by using Korsmeyer–Peppa's equation. Since the "n" value of optimized formulation F8 was 0.49, which is between "0.45 to 0.85" it indicates that the drug

release depends on swelling, diffusion, and erosion. All formulations follow the non-Fickian/anomalous type of diffusion.

CONCLUSION: Floating Drug Delivery System assist in improving the oral controlled delivery of drugs that have an absorption window in the particular region of the GI tract by retained in the stomach for a longer time and as well as for controlling the release of the drug having site-specific absorption limitation. Venlafaxine Hcl is an extremely effective antidepressant drug used to develop a controlled release formulation. Venlafaxine Hcl exhibits pH-dependent solubility. It is more soluble in acidic pH and slightly soluble at neutral or alkaline conditions (intestinal environment). Hence, an attempt was made to develop gastro retentive delivery system of Venlafaxine HCl, which increased the bioavailability of Venlafaxine HCl and also to reduce the frequency of administration, thereby improving patient compliance and therapeutic efficacy. The drug release and floating properties of the prepared tablets were influenced by the drug-polymer ratios and the viscosity of polymers. From the results, it can be concluded that as the concentration of the polymer increased, floating lag time decreased and the percentage drug release was also prolonged. The viscosity of the polymer also showed a directly proportional relationship with the swelling characteristics of the tablets.

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