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FORMULATION DEVELOPMENT AND INVITRO EVALUATION OF GASTRO RETENTIVE DESVENLAFAXINE HYDROCHLORIDE FLOATING TABLETS

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ABSTRACT

Floating Drug Delivery System are retained in the stomach for a longer time and assist in improving the oral controlled delivery of drugs that have an absorption window in the particular region of the GI tract as well as for controllingthe release of the drug having site-specific absorption limitation. Desvenlafaxine HCl is a highly effective antidepressant was used as a modeldrug to develop a controlled release formulation. Desvenlafaxine HCl exhibits pH dependent solubility. It is more soluble in acidic pH and slightly soluble at neutral or alkaline condition (intestinal environment). Hence an attempt was made to develop gastroretentive delivery system of Desvenlafaxine HCl which increased the bioavailability of Desvenlafaxine HCl and also to reduce frequency of administration, thereby improving patient compliance and therapeutic efficacy.

KEYWORDS: Floating Drug Delivery System, Desvenlafaxine HCl, antidepressant.

INTRODUCTION

The design of an oral controlled drug delivery system (DDS) should be primarily aimed at achieving more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, such as an inability to restrain and localize the DDS within desired regions of the gastrointestinal (GI) tract and the highly variable nature of the gastric emptying process. It can be anticipated that, depending upon the physiological state of the subject and the design of the pharmaceutical formulation, the emptying process can last from a few minutes to 12 hours (hr). This variability in turn may lead to unpredictable bioavailability and times to achieve peak plasma levels since the majority of drugs are preferentially absorbed in the upper part of the small intestine. Furthermore, the relatively brief gastric emptying time (GET) in humans, which normally averages 2–3 hr through the major absorption zone (stomach or upper part of the intestine), can result in incomplete drug release from the DDS leading to diminished efficacy of the administered dose. Thus, control of the placement of a DDS in a specific region of the GI tract offers numerous advantages, especially for drugs exhibiting an absorption window in the GI tract or drugs with a stability problem. Overall, the intimate contact of the DDS with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption. These considerations have led to the development of oral controlled-release (CR) dosage forms possessing gastric retention capabilities.[1]

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.[2]

O-desmethyl Desvenlafaxine is a tertiary amino compound that is N,N-dimethylethanamine substituted at position 1 by a 1-hydroxycyclohexyl and 4-hydroxyphenyl group. It is a metabolite of the drug Desvenlafaxine. It has a role as a marine xenobiotic metabolite, a drug metabolite and an antidepressant. It is a member of cyclohexanols, a member of phenols and a tertiary amino compound. it is chemicallay called as 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl) ethyl] phenol.[3]

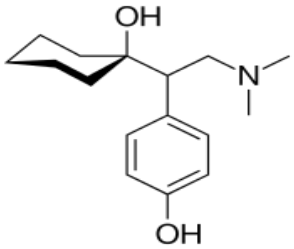

Figure 1: Chemical structure of Desvenlafaxine.

Experimental work

Materials

Desvenlafaxine HCl collected from Aurabindo pharma, Carbopol 934p and Xanthan gum from Himedia laboratories, Sodium bicarbonate and Talc from Nice laboratories, Magnesium Stearate and MCC from S.D fine chemicals. All the instruments were used in the work was calibrated.

Methodology

Preformulation Studies

Organoleptic Properties

Colour: Take a small quantity of sample and spread it on the white paper and examinetvisually.

Physical Properties

Angle of repose

Determinations of bulk density and tapped density

Compressibility index

Melting point

Solubility

Drug-excipient compatibility studies

Procedure by FT-IR studies

The FT-IR studies are conducted for Desvenlafaxine HCL and mixture of Desvenlafaxine HCL and excipients by preparing dispersion in potassium bromide discs. The peaks are obtained and compared with the standards by superimposing these spectra and observed for any difference in shape and size of spectrum. If there is any significant change represents interaction between drug and excipients.

PREPARATION OF STANDARD CURVE

DETERMINATION OF λmax OF Desvenlafaxine Hcl IN ACID BUFFER (pH 1.2)

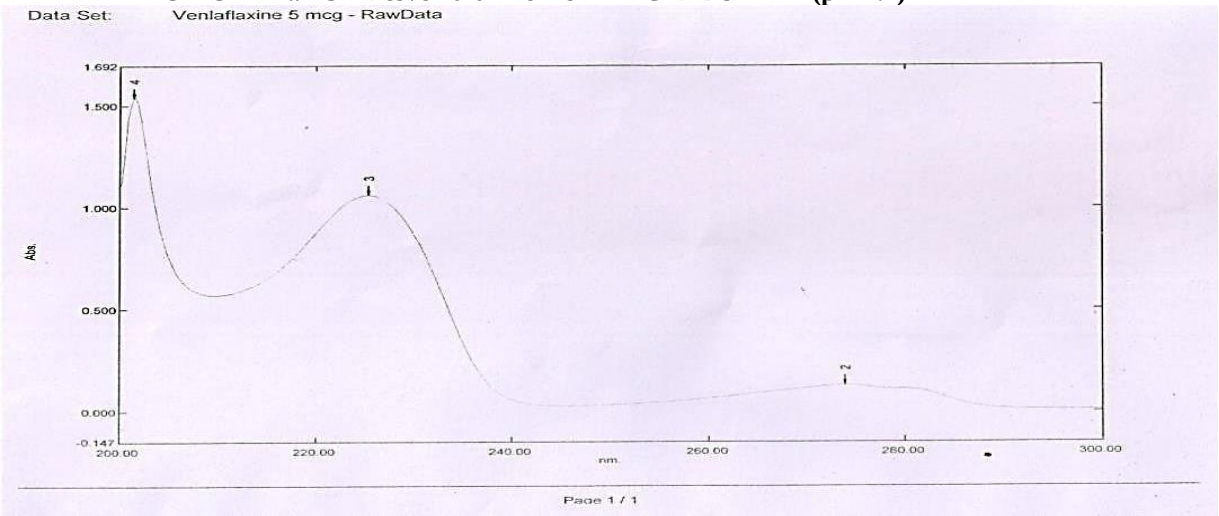

Figure 2: Spectrum of Desvenlafaxine HCl.

Desvenlafaxine HCl drug solution in pH 1.2(0.1N HCl) was scanned using UV- Spectrophotometer between the range 210-400nm using pH 1.2 as blank and the maximum absorbance (λ max) was found at **224nm.**

Preparation of 0.1 M Hydrochloric acid

Accurately measure 8.5 ml of hydrochloric acid and sufficient water to make upto 1000 ml.

Preparation of stock solution

Accurately weigh 100 mg of Desvenlafaxine HCL and transfer it to a 100 ml volumetric flask. Then make up the volume to 100 ml with 0.1 M Hcl.

Preparation of standard solution

Pipette out 10 ml of the above solution and transfer it to a 100 ml volumetric flask. Then make up the volume to 100 ml with 0.1 M Hcl. Then from the standard stock solution withdraw 2ml, 4ml, 6ml, 8ml, and 10ml into five 100 ml different volumetric flasks. Then make up the volume to 100 ml with 0.1M Hcl to get 2, 4, 6, 8,10 µg/ml concentration.

CALIBRATION CURVE OF DESVENLAFAXINE HCL

The absorbance of the prepared stock solutions was measured at 224 nm in an UV spectrophotometer. Plot a graph between concentration (in µg/ml) V/S absorbance (in nm) on X-axis and Y-axis respectively.

Table 1: Calibration curve of Desvenlafaxine HCL.

S.no.	Concentration (in µg/ml)	Absorbance (in nm)
1.	0	0.000
2.	2	0.136
3.	4	0.305
4.	6	0.462
5.	8	0.612
6.	10	0.759
R^2	0.9997	

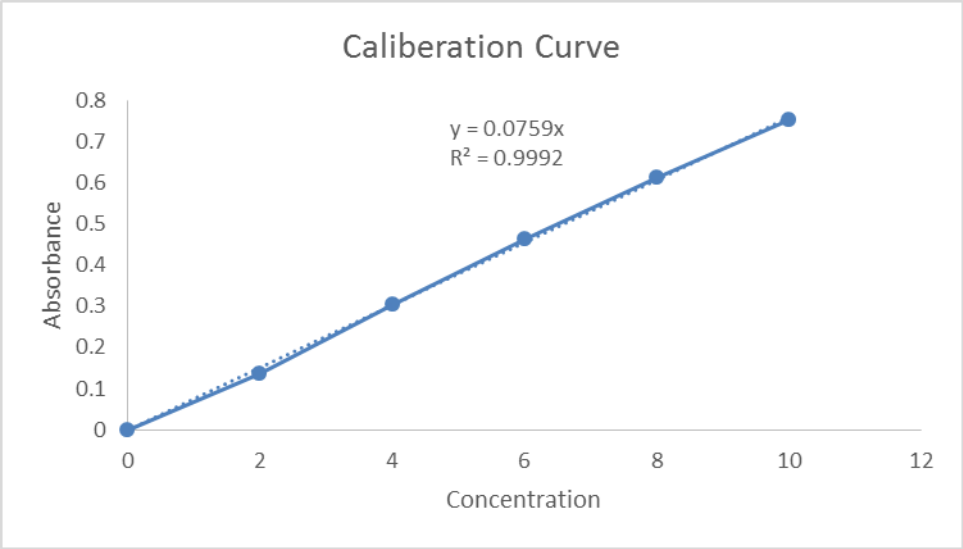

Figure 3: calibration curve of Desvenlafaxine HCL.

Table No. 2: The Composition of Tablets Prepared Using Desvenlafaxine HCl.

INGREDIENTS / FORMULATION	F1	F2	F3	F4	F5	F6	F7	F8	F9
Desvenlafaxine HCl	150	150	150	150	150	150	150	150	150
Carbopol 934p	20	25	30	-	-	-	-	-	-
Xanthan gum	-	-	-	80	95	110	-	-	-
HPMC K100M	-	-	-	-	-	-	60	70	80
Sodium bicarbonate	7	7	7	7	7	7	7	7	7
MCC	147	142	137	87	72	57	107	97	87
MagnesiumStearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Total	330	330	330	330	330	330	330	330	330

STEPS INVOLVED IN FORMULATION

Each tablet containing 300 mg Desvenlafaxine HCl were prepared by direct compression method. Accurately weighed amount of drug Desvenlafaxine HCl, Carbopol 934 p, Xanthan gum, HPMC K100M, PEO, Sodium CMC were mixed geometrically in a mortar. Then binder PVP K 30, MCC, Sodium bicarbonate, Sodium bicarbonate and MCC are passed through the sieve and thoroughly mixed for 15 minutes. The powder blend then lubricated with Talc and magnesium stearate for 2 minutes and compressed on a tablet punching machine using 9 mm punches. The totalweight of the tablet is 330 mg.

EVALUATION

Pre-compression parameters.
Angle of repose.
Bulk density and Tapped density.
Compressibility index and Hausner ratio.

Evaluation Of Formulated Tablets of Desvenlafaxine Hcl

All the formulated sustained release tablets were evaluated for following official and unofficial parameters.

Assay

Crush 20 tablets and weigh equivalent to 20 mg Desvenlafaxine HCL and dissolved in 0.1N Hcl and

make up the volume to 100 ml. From that, withdraw 10 ml and diluted to 100 ml with 0.1 N Hcl. Read the absorbance at 232 nm in UV spectrophotometer.

Kinetics of drug release

The invitro dissolution profile of all batches were fitted to Zero order, first order, Higuchi model and Koresmeyer-Peppas model to ascertain the kinetic modeling of drug release. Correlation coefficient (R^2) values were calculated for linear curves obtained by the regression analysis of the above plot.

Zero-order kinetic model – Cumulative % drug released Vs time.

First-order kinetic model – log cumulative % drug remaining Vs time.

Higuchi model - Cumulative % drug released Vs square root of time.

Korsmeyer-Peppas model - log cumulative % drug released Vs logtime.

When data is plotted as log cumulative % remaining Vs time yields a straightline, and then the release obeys first order kinetics. The constant 'K' obtained by multiplying 2.303 with the slope values.

RESULT AND DISCUSSION

Preformulation studies

Organoleptic properties

Colour- Crystalline solid, White to off-white.

Odour- Odourless.

Physical properties

Angle of repose

Material	Angle of repose
Desvenlafaxine HCl	27.230

The results show that the drug having poor flow.

Bulk density and tapped density

Material	Bulk density (gm/ml)	Tapped density(gm/ml)
Desvenlafaxine HCl	0.53	0.56

Powder compressibility

Material	Compressibility index	Hausner's ratio
Desvenlafaxine HCl	6.84	1.06

Melting point

Material	Melting point range	Result
Desvenlafaxine HCl	215-217^{0}c	215^{0}c

The result indicates that the Desvenlafaxine HCl drug was pure one.

SOLUTION PROPERTIES

Solubility

Material	Test	Specification	observation
Desvenlafaxine HCl	Solubility	soluble in water, DMSO	Complies

FTIR STUDIES

Table 3: Compatibility Studies of Desvenlafaxine HCl with Excipients.

S. NO	Excipients	Drug/ Excipients Ratio	Physical DescriptionInitial	35^{0}C ± 2^{0}C / 60% ± 5% RH		
				1Week	2Week	3Week
1	Desvenlafaxine HCl	-	White crystalline powder	*	*	*
2	Drug + carbopol934	1:1	White crystalline powder	*	*	*
3	Drug + xanthangum	1:1	White crystalline powder	*	*	*
4	Drug + HPMCk100M	1:1	White crystallinepowder	*	*	*

*** indicates no incompatibility**.

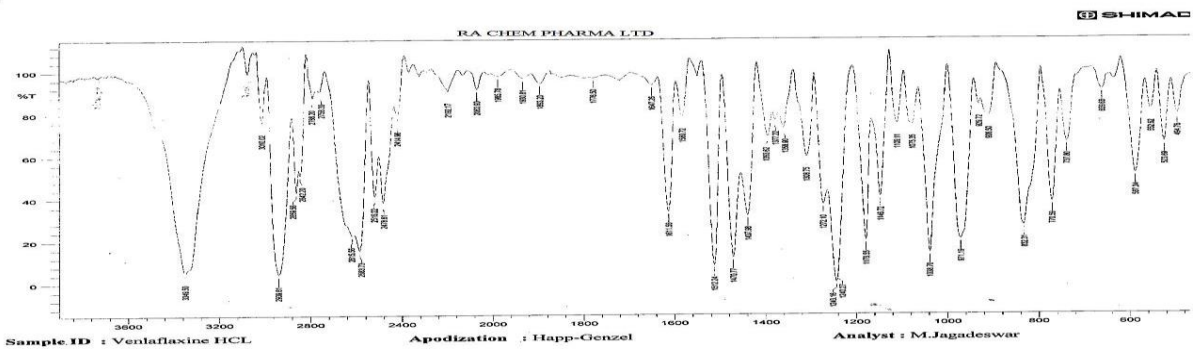

Figure 4: FTIR Spectroscopy of pure drug.

Evaluation Parameters

Pre Compression Parameters

Table 4: Evaluation parameters of powder blend.

Formulation	Angle of repose	Bulk density(gm/cc)	Tapped density(gm/cc)	Compressibility index (%)
F1	$29^0 1^1 \pm 0.1$	0.36±0.004	0.41±0.018	11.8±0.8
F2	$30^0 3^1 \pm 0.2$	0.37±0.001	0.44±0.017	13.4±0.8
F3	$32^0 1^1 \pm 0.5$	0.38±0.005	0.44±0.004	13.3±0.6
F4	$30^0 6^1 \pm 0.3$	0.35±0.005	0.41±0.003	14.2±1.4
F5	$32^0 8^1 \pm 0.5$	0.34±0.004	0.40±0.018	14.8±1.2
F6	$33^0 8^1 \pm 0.1$	0.35±0.002	0.42±0.001	16.2±0.7
F7	$28^0 1^1 \pm 0.7$	0.35±0.002	0.40±0.005	12.6±0.9
F8	$28^0 5^1 \pm 0.3$	0.36±0.003	0.41±0.002	12.7±1.1
F9	$31^0 2^1 \pm 0.1$	0.36±0.005	0.42±0.004	14.2±1.3

Floating tablets of Desvenlafaxine HCl was developed to increase the gastric residence time of the drug, so that they can be retained in the stomach for longer time and help in controlled release of drug up to 12 hrs. Different grades of viscosities of Carbopol 934, xanthan gum, HPMC K100M polymers is known to be beneficial in improving floating property and release characteristics.

The pre- compression parameters obtained for all formulations are tableted in the table no 3. The value of angle of repose was found to be in the range of $28^0 1^1$ to $33^0 8^1$. This indicates good flow property of powder blend. Carr's index value ranges between 11.8 to 16.2% indicates that the powder blend have the required flow property for direct compression.

Table 4: Post Compression Parameters.

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Averageweight variation(mg)	Drug content (%)
F1	3.76±0.04	5.33±0.02	0.65±0.07	331.2±1.3	98.06
F2	3.68±0.07	5.61±0.05	0.59±0.09	330.7±1.4	98.39
F3	3.62±0.02	5.44±0.03	0.53±0.05	331.5±1.7	97.22
F4	3.71±0.04	5.48±0.01	0.54±0.11	330.2±2.1	99.02
F5	3.67±0.09	5.86±0.04	0.47±0.08	329.8±2.3	97.18
F6	3.63±0.11	6.14±0.02	0.47±0.12	331.3±2.1	97.56
F7	3.74±0.02	5.42±0.03	0.57±0.04	329.2±1.4	97.19
F8	3.76±0.01	5.57±0.01	0.54±0.07	328.7±1.8	98.45
F9	3.69±0.05	5.72±0.05	0.53±0.06	331.4±1.2	98.28

The floating tablets were prepared by direct compression method using the polymers Carbopol 934, Xanthan gum, HPMC K100M to provide sufficient drug release retardation and provide sufficient buoyancy to the tablets. The prepared floating tablets were evaluated for thickness, hardness, friability, average weight variation, drug content, all the studies were performed intriplicates and the results were expressed in ± standard deviation. The measured hardness for the tablets for each batch arranged between 5.33 to 6.14 kg/cm, this ensures the good handling characteristics of all the batches.

The % friability was less than 1% in all the formulations ensuring that thetablets were mechanically stable. The weight variation for different formulations was found to be 328.7 to331.4, indicates consistency in each batch. The drug content was found to be 97.19 to 98.45, with low standard deviation indicates batch to batch consistency.

SWELLING INDEX

Table 5: Swelling index (%) of formulations.

Time (hrs)	Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	26.6	23.3	22.8	40.7	37.2	36.4	17.8	19.4	22.1
2	87.45	74.77	41.2	73.25	74.5	68	34.7	36.1	36.5
4	158.8	149.7	65.7	163.7	160.3	130.7	59.4	64.2	72.3
6		154.5	114.8			154.2	89.2	98.2	112.7
8			133.4				122.3	114.5	128.7
10								126.9	132.3
12									135.1

Swelling index for all the formulations was carried out in the 0.1N HCl. The formulations showed different indices in the swelling media and it is shown in the table. Tablets containing carbopol934 and HPMC K100M showed maximum swellingin 12 hr with sharp increase up to 8 hr this may due to increased concentration of HPMC K100M which retain water and form thick swollen mass.

BUOYANCY STUDIES

Table no. 6: Buoyancy studies of formulations.

Formulation code	Floating lag time (sec)	Floating duration (hrs)
F1	52	4.5
F2	58	6
F3	76	8
F4	29	4.5
F5	36	5
F6	34	6.5
F7	34	8.5
F8	32	10
F9	39	12

The *in-vitro* floating behavior of the tablets was studied by placing them in beaker containing 0.1 N HCl (pH 1.2). The gas generating agents immediately evolves carbon dioxide in presence of HCl solution generating sufficient porosity which helped the dosage unit to float. Formulation F1-F3 prepared with carbopol934p started floating after 52 seconds and remains buoyant for 8 hr till they were completely eroded.

- On the other hand formulation F4-F6 prepared with Xanthan gum whichshows a floating time of 6.5 hrs and formulation of F7-F9 prepared with HPMC K100M show decrease in floating lag time to 34 seconds and increased floating duration time to 12 hrs. This might be due to high viscosity polymer HPMC K100M maintains the integrity of the tablets for longer duration by reducing the effect of erosion thus resulting in increase in floating time. The results are shown in table no. 6. Thus it can be concluded that the batch containing HPMC polymers showed good floating lag time and total floating time.

***In-Vitro* DRUG RELEASE STUDIES**

In-vitro drug release studies were carried out using USP dissolution apparatus type II at 50 rpm. The dissolution medium consisted of 900 ml of pH 1.2 acid buffer (0.1N HCl), maintained at 37 $\pm$ 0.5^0C. The drug release at different time intervals wasmeasured using an ultraviolet visible spectrophotometer at 224 nm.

Table no.7: Percentage drug release of formulations.

Time (hrs)	Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	24.87	22.92	20.06	38.34	32.28	27.54	23.46	22.43	18.84
2	58.16	55.27	48.07	62.15	45.38	41.15	39.87	31.11	24.18
4	96.53	71.18	69.18	98.1	94.19	76.77	67.82	53.67	43.67
6		96.11	78.92			96.13	82.09	65.28	61.08
8			98.33				97.12	76.59	72.49
10								98.76	83.54
12									98.03

In-vitro dissolution studies were performed for all the formulations using USP dissolution apparatus II at 50 rpm using 900 ml of 0.1N HCl as dissolution medium. The samples withdrawn and were analyzed by using UV spectrophotometer. The drug release from the formulations F1-F3 prepared with Carbopol 934P was found to be 96.53, 93.11 and 98.33%, where as formulation F4- F6 prepared with Xanthan gum was found to be 98.1, 94.19, 96.13 at the end of 4 & 6 hours. Formulations F7-F9 prepared with HPMCK100M was found to be 97.12, 98.76, 98.03% showed reasonable drug release of formulation in F9. As per the results of dissolution study the formulations F1-F9 the drug release was sustained for 4 to 12hr.

All the formulations were designed as dosage form for 12 hours. In order to check the 100% dissolution release profile, formulations were subjected to dissolution studies for 12 hours. Among the nine formulations F9 was best and shows 98.03% drug release in the end of 12 hours. It is evident from the *in-vitro* dissolution data that increase in HPMC K100M concentration decreases the release rate this might be due to increase in diffusional path length, which the drug molecule may have to travel. So, formulation F9 was selected as the optimized formulation.

RELEASE KINETICS

Table No. 8 Model fitting for formulation F_9.

Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released
0	0	100	0.000	2.000	0.000	0.000
1	**18.84**	81.16	1.414	1.909	0.301	1.275
2	**24.18**	75.82	2.000	1.880	0.602	1.383
4	**43.67**	56.33	2.449	1.751	0.778	1.640
6	**61.08**	38.92	2.828	1.590	0.903	1.786
8	**72.49**	27.51	3.162	1.439	1.000	1.860
10	**83.54**	16.46	3.464	1.216	1.079	1.922
12	**98.03**	1.97	3.464	0.294	1.079	1.991

The mechanism of drug release is predicted by using Korsmeyer–Peppas equation. The n value of optimized formulation F9 is 0.66 respectively and is between “0.45 to 0.85”. This indicates that the drug release depends on swelling, diffusion, and erosion. All formulations follow the non- Fickian/anomalous type of diffusion.

STABILITY STUDIES

Table 9: floating lag time.

Time (days)	$25^oC \pm 2^oC/60\% RH \pm 5\% RH$, $30^oC \pm 2^oC/65\% RH \pm 5\% RH$, $40^oC \pm 2^oC/75\% RH \pm 5\% RH$			
	Hardness (kg/cm^2)	Drug content (%)	% Drug release	Total floating time
30	5.56	98.45	98.34	>12
60	5.56	98.42	98.27	>12
90	5.48	98.18	98.71	>12

Stability studies were carried out on selected formulations (F9) as per ICH guidelines. There was not much variation in matrix integrity of the tablets at all the temperature conditions. There was no significant changes in drug content, physical stability, hardness, friability, drug release, floating lag time (Table 9) for the selected formulation F8 after 90 days at $25^oC \pm 2^0C$ / 60% ± 5% RH, $30^0C \pm 2^0C$ / 65% ±5% RH and $40^0C \pm 2^0$ / 75% ± 5% RH.

SUMMARY

In the present work, 9 different formulations were prepared by direct compression, incorporating polymers like Carbopol934, Xanthan gum and HPMC K100M as swelling polymers, sodium bicarbonate as gas generating agent, MCC as a diluents, talc used as glidant and magnesium stearate used as lubricant.

Characterization of the drug was done by performing the UV spectroscopy and IR spectroscopy. IR spectrum of the pure drug was compared with that of physical mixture of drug with all the excipients used in the study. The results showed that there was no drug-excipient interaction. The UV spectral analysis of the drug solution indicated that λmax value as 224 nm.

All the prepared floating formulations were evaluated for hardness, friability, uniformity of weight, drug content uniformity, drug-polymer interaction, *in-vitro* floating studies, *in vitro* drug release and short term stability studies. The thickness of the formulations (F1-F9) was in the range of 3.62 ± 0.03 to 3.71 ± 0.05mm and the

hardness was in the range of 5.3 ± 0.2 to 6.1 ± 0.3 Kg/ cm^2,indicated good mechanical strength of the tablets. Friability, weight variation anddrug content uniformity was found to be within official limits for all the formulations.

The dissolution studies were carried out for 12 hrs. As per the result of dissolution study formulation F7, F8 and F9 showed reasonable release respectively. But F9 showed good floating lag time and total floating time, when compare to other formulations. Based on all these results, formulation F9 was selected as the optimized formulation. F9 was then compared to the marketed product and was found that the optimized formulation F9 has better control over release rate in comparison to the commercial product.

The release kinetics were fitted to different mathematical models like Zero order, First order, Higuchi's and Peppa's plot. The selected formulation F9 follows Higuchi's plot and slope (*n*) value of Peppa's for these formulations were found to be in the range of "0.45 to 0.85". This indicates that the drug release depends on swelling, erosion, and diffusion. Thus follows the non-Fickian/anomalous type ofdiffusion.

The drug-polymer ratios, viscosity of polymers, were found to influence the drug release and floating properties of the prepared tablets. 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 prolonged. Viscosity of the polymer also showed a directly proportional relationship with swelling characteristics of the tablets. The optimized formulation (F9) was subjected for stability studies as per ICH guidelines. Formulations subjected for short term stability studies were checked for drug content, hardness, friability and Total floating time for 90 days with an interval of 15 days. The formulations were found to be stable as no significant change was observed in the various evaluated parameters of the formulations.

CONCLUSION

Floating Drug Delivery System are retained in the stomach for a longer time and assist in improving the oral controlled delivery of drugs that have an absorption window in the particular region of the GI tract as well as for controlling the release of the drug having site-specific absorption limitation. Desvenlafaxine HCl is a highly effective antidepressant was used as a modeldrug to develop a controlled release formulation. Desvenlafaxine HCl exhibits pH dependent solubility. It is more soluble in acidic pH and slightly soluble at neutral or alkaline condition (intestinal environment). Hence an attempt was made to develop gastroretentive delivery system of Desvenlafaxine HCl which increased the bioavailability of Desvenlafaxine HCl and also to reduce frequency of administration, thereby improving patient compliance and therapeutic efficacy.

REFERENCE

1. Neha narang. An updated review on floating drug delivery system. IJPR, 2011; 3(1): 1-7.
2. Garg, R. and Gupta G.D., Progress in controlled gastroretentive delivery systems. Trop J Pharm Res, 2008; 7(3): 1055- 1066.
3. https://pubchem.ncbi.nlm.nih.gov/compound/Desvenlafaxine.
4. H L Sharma, K K Shrma. The textbook "principle of pharmacology", 2nd edition, 2010.
5. Government of India, Ministry of health and family welfare, The Indian Pharmacopoeia commission, Ghaziabad; The Indian Pharmacopoeia, 2007; 3.
6. Marabathuni VJ, Dinesh P, Ravikumar R, Yamini P, Kiran PS, Hussain SP, Rao CM. Chitosan based sustained release mucoadhesive buccal patches containing amlodipine besylate (AMB). Asian J Res Pharm Sci, 2017 Jun 28; 7: 97-104.
7. Marabathuni VJ, Bhavani M, Lavanya M, Padmaja K, Madhavi N, Babu P, Rao CM. Formulation and evaluation of mouth dissolving Tablets of carbamazepine. Asian Journal of Pharmacy and Technology, 2017; 7(3): 137-43.