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FORMULATION AND EVALUATION OF RAPIDLY ORO-DISPERSIBLE TABLET CONTAINING VENLAFAXINE HYDROCHLORIDE FOR THE TREATMENT OF ANXIETY

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Keywords:

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ABSTRACT: Purpose: The main purpose was to develop Oro-dispersible tablet to overcome the problem of dysphagia which is common in pediatric, geriatric and unconscious patients. **Method:** The Oro-dispersible tablets were prepared by direct compression method by using two different individual superdisintegrant like Sodium Starch Glycolate and Crospovidone as well as combination of superdisintegrant with newly marketed filler-binder Isomalt were used. Friability, disintegration time and percent drug release were taken as dependent variable. The excipients were used like Avicel as directly compressible excipient, Talc and Magnesium Stearate as lubricant, Sodium Saccharine and Mannitol as sweetening agent. The tablets were evaluated for hardness, friability, thickness, weight variation, wetting time, water absorption ratio, disintegration time and *in-vitro* drug release study. Venlafaxine hydrochloride, commonly used as anti-hypertensive and has anxiolytic property, poor bioavailability due to extensive first pass metabolism. **Results:** It was observed that hardness of all tablets was 3.13-4.11 Kg/cm^2, friability of all formulation was found to be less than 1%, Weight variation was as per the USP specification and maximum % drug release of optimized batch containing super disintegrating agent Sodium Starch Glycolate was 87.71% in 60 min. **Conclusion:** it was concluded that developed Oro-dispersible tablet of Venlafaxine hydrochloride by using superdisintegrant dissolves rapidly in mouth also drawn a comparative study between the effect of the used excipients on pharmacokinetic parameters like *in-vitro* drug release and bioavailability.

INTRODUCTION: For both solid and liquid dosage forms, oral administration is the most frequent and recommended method of drug administration.

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But the convenience of administration, precise dosage, self-medication, pain avoidance and most crucially patient compliance, make solid dosage forms appealing [1].

Oro-dispersible tablets are those that easily dissolve in the mouth before being swallowed, according to the European Pharmacopoeia. Oro-dispersible tablets (ODTs) are "a solid dosage form containing a medical component or active ingredient which disintegrates fast usually within a couple of

seconds when placed on the tongue." According to the United States Food and Drug Administration, ODTs typically disintegrate in a period of time between a few seconds and a minute [2]. The first ODTs were designed to make taking vitamins more enjoyable for children by disintegrating through effervescence instead of dissolving [3]. The technique was adapted to pharmaceuticals with the invention of microparticles containing drugs. These microparticles would be released upon effervescence of the tablet and swallowed by patient [4]. Dissolution became more effective than effervescence through improved manufacturing processes and ingredients such as the addition of mannitol to increase binding and decrease dissolution time [5-10].

Venlafaxine hydrochloride is a novel antidepressant. It is a white crystalline solid and freely soluble in water. The recommended dose for Venlafaxine hydrochloride ranges from 75 to 350mg per day. Drug Venlafaxine is a known serotonin norepinephrine reuptake inhibitor (SNRI) [11-12]. It works by blocking the reabsorption (or reuptake) of serotonin and norepinephrine back into the nerve cells that released them, which increases the levels of active neurotransmitters in the brain, thereby, uplifting one's mood and energy by treating depression, anxiety or other underlying issues. Venlafaxine hydrochloride has poor bioavailability of 40-50%. It shows 92% oral absorption and 12.6% drug reaches to systemic circulation due to first pass metabolism. The steady state half-life of Venlafaxine hydrochloride and its active metabolite (O-Desmethyl Venlafaxine) is 5 h and 11 h respectively [12-13].

The short half-life of this drug allows it to be formulated in the form of immediate release dosage forms like Oro-dispersible tablets. Oro-dispersible tablets give rapid onset of action making them the preferred choice of medication in treating hypertension, anxiety attacks, or other conditions which need quick treatment. Therefore, an attempt was made to prepare rapidly dissolving tablet of Venlafaxine hydrochloride by using superdisintegrant [14-15].

Ideal Properties of Oro-dispersible Tablets [16]:

1. Tablets should break down or disintegrate in the mouth in a matter of seconds.
2. Water shouldn't be necessary for them to dissolve or to get absorbed.
3. Tablets must have a satisfying mouth feel.

Mechanism of ODTs [16-19]: To accomplish the desired quick dissolving properties, ODTs use the following mechanisms:

1. For the tablet to instantly disintegrate and rapidly dissolve, water must enter the tablet matrix quickly.
2. The addition of highly water-soluble excipients or a suitable disintegrating agent to the tablet formulation.
3. The tablet is broken down into tiny particles by the stated mechanisms, which then forms a solution or suspension of the medication. The three mechanisms include -

- Capillary action,
- Chemical reaction,
- High swellability of disintegration.

MATERIAL AND METHOD: Venlafaxine Hydrochloride was provided by Hikal Ltd., Banglore, India as a gift sample. Isomalt was provided by SFA Food and Pharma Ingredients Pvt. Ltd., Thane, India as a gift sample. Avicel, Crospovidone, Sodium Starch Glycolate, Sodium Saccharin, Mannitol, Talc, Magnesium Stearate and Orange Flavor were supplied by Research-Lab Fine Chemical Industries, Mumbai, India.

Method:

Preparation of Venlafaxine Hydrochloride Oro-Dispersible Tablets [20-25]: The Oro-dispersible tablets were prepared by using Venlafaxine hydrochloride as Active Pharmaceutical Ingredient, Crospovidone and Sodium Starch Glycolate as superdisintegrants, Avicel as directly compressible excipient, Talc and Magnesium Stearate as lubricant, Sodium Saccharine and Mannitol as sweetening agent, Isomalt as multifunctioning excipient and flavoring agent. The specified quantity of drug and other excipients were weighed accurately. API, Superdisintegrant, Directly Compressible excipient sifted through 40# mesh separately prior to mixing, resulting all powders including talc, magnesium stearate, sodium saccharine and orange flavor were transferred to

mortar in geometrical order and triturated. The final blend was sifted through 40# mesh. Then the final blend was compressed into tablets by using Single punch tablet compression machine. The different batches for the preparation of Venlafaxine hydrochloride tablets were shown in **Table 1.**

TABLE 1: FORMULATION TABLE OF VENLAFAXINE HYDROCHLORIDE ORO-DISPERSIBLE TABLETS

Ingredients	Quantity of Ingredients (mg) for One Tablet											
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12
Venlafaxine hydrochloride	25	25	25	25	25	25	25	25	25	25	25	25
Crospovidone	25	35	45	-	-	-	25	35	45	-	-	-
Sodium Starch Glycolate	-	-	-	25	35	45	-	-	-	25	35	45
Isomalt	-	-	-	-	-	-	190	180	170	190	180	170
Mannitol	138.75	128.75	118.75	138.75	128.75	118.75	-	-	-	-	-	-
Avicel	50	50	50	50	50	50	-	-	-	-	-	-
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Orange Flavor	5	5	5	5	5	5	5	5	5	5	5	5
Sodium Saccharine	1.25	1.25	1.25	1.25	1.25	1.25	-	-	-	-	-	-
Total Weight	250	250	250	250	250	250	250	250	250	250	250	250

Experimental Study:

Standard Calibration Curve of Venlafaxine hydrochloride in Phosphate Buffer pH 6.8 [26-27]: 100mg of Venlafaxine hydrochloride was weighed and dissolved in 100 ml of phosphate buffer pH 6.8.10ml solution was withdrawn and diluted to 100 ml with phosphate buffer pH 6.8. Further dilution was made by withdrawing 10 ml solution and diluted to 100ml with Phosphate Buffer pH 6.8 to get a 10 µg/ml stock solution of Venlafaxine hydrochloride.

From this stock solution 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 ml solution was withdrawn and diluted up to 10 ml to get 1-10 µg/ml respectively. Absorbance was taken on UV visible spectrophotometer at λmax 225 nm. The linear plot was constructed, and correlation coefficient value was determined.

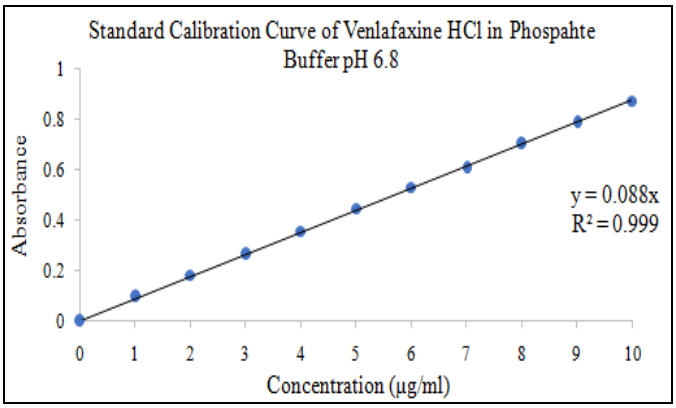

FIG. 1: STANDARD CALIBRATION CURVE OF VENLAFAXINE HCL IN PHOSPHATE BUFFER pH 6.8

Solubility of Venlafaxine hydrochloride

Solubility of Drug in Water: 10 mg of drug was added in 100ml of water in a beaker and kept on Magnetic Stirrer at room temperature at 150-200 rpm for 24 hours. After 24 hours, absorbance was measured on UV Spectrophotometer at 225nm wavelength.

Solubility of Drug in Phosphate Buffer pH 6.8 [27]: 10mg of drug was added in 100ml of Phosphate Buffer pH6.8 in a beaker and kept on Magnetic Stirrer at room temperature at 150-200 rpm for 24 hours. After 24 hours, absorbance was measured on UV Spectrophotometer at 225nm wavelength.

TABLE 2: SOLUBILITY OF VENLAFAXINE HYDROCHLORIDE IN WATER AND PHOSPHATE BUFFER pH 6.8

Solvent	Concentration (µg/ml)
Water	9.84± 0.07
Phosphate Buffer pH 6.8	9.35 ± 0.02

Each value represents the mean ± standard deviation (n=3)

Evaluation Parameters:

Pre-Compression Parameters:

Angle of Repose*:* Angle of repose was determined by using funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of powder blend. Accurately weighed powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the pile was measured and angle of repose was calculated.

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

Where h = height of the pile, r = radius of the pile.

Bulk Density: Apparent bulk density was determined by pouring a weighed quantity of powder blend into graduated cylinder and measuring the volume and weight. Bulk density was calculated by using the following formula.

Bulk Density = Weight of the Powder (g) / Volume of the Packing (ml)

Tapped Density: Tapped density was determined by placing a graduated cylinder, containing a known mass of powder blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10 cm at 2 second intervals for 5 minutes. The tapping continued until no further change in volume was noted. Tapped density was calculated by using following formula:

Tapped Density = Weight of the Powder (g) / Volume of the Tapped Powder (ml)

Compressibility Index: Compressibility index was the measure of the powder's ability to be compressed. The Compressibility Index of the powder blend was determined from bulk density and tapped density. Compressibility Index was calculated by using following formula:

% Compressibility Index = (Tapped Density – Bulk Density) × 100 / Tapped Density

Hausner's Ratio [24-26]: Hausner's ratio was determines the flowability of powder material. Hausner's ratio was calculated by using following formula:

Hausner's Ratio = Tapped Density / Poured Density

Hausner's Ratio <1.25 – Good flow with 20% Compressibility Index.

Hausner's Ratio >1.25 – Poor flow with 33% Compressibility Index.

TABLE 3: PRE-COMPRESSION RESULTS OF POWDER BLEND

Batch	Angle of Repose (°)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio
B1	28.92±0.09	0.396±0.06	0.456±0.06	13.15±0.08	1.15±0.04
B2	30.46±0.06	0.362±0.09	0.416±0.08	12.98±0.09	1.14±0.07
B3	30.07±0.09	0.409±0.07	0.462±0.05	11.47±0.06	1.12±0.05
B4	36.10±0.03	0.403±0.08	0.480±0.04	16.04±0.04	1.19±0.09
B5	33.86±0.07	0.461±0.03	0.536±0.09	30.08±0.03	1.14±0.07
B6	28.46±0.05	0.416±0.02	0.595±0.07	12.35±0.01	1.43±0.02
B7	29.72±0.04	0.437±0.06	0.508±0.02	13.97±0.02	1.16±0.01
B8	25.17±0.09	0.432±0.07	0.506±0.04	17.98±0.05	1.17±0.06
B9	28.63±0.01	0.402±0.05	0.502±0.06	19.92±0.06	1.20±0.08
B10	30.76±0.03	0.400±0.01	0.498±0.05	19.67±0.08	1.24±0.03
B11	34.16±0.07	0.399±0.06	0.506±0.01	22.33±0.09	1.26±0.09
B12	32.09±0.05	0.389±0.04	0.494±0.02	21.25±0.01	1.28±0.01

Each value represents the mean + standard deviation (n=3).

Post Compression Parameters: All the formulated ODTs were subjected to the following quality control tests:

Weight Variation*:* The weight variation test was carried out to ensure uniformity in the weight of tablets in each batch. 20 tablets from each batch were collected, weighed and the average weight was calculated. The individual weight of each tablet was also determined to find out the weight variation.

Hardness: The hardness of tablet was an indication of its strength. Measuring the force required to break the tablet across tests it. The force was measured in Kg/cm^2. The hardness of about 3-5 Kg/cm^2 was satisfactory for uncoated tablets. Hardness of tablet was determined by Monsanto hardness tester.

Thickness: Tablet thickness was determined by the amount of fill permitted to enter the die cavity, the compaction characteristics of the fill material and the force or pressure applied during compression.

Tablet thickness was measured with a Vernier caliper. The thickness of a tablet should be controlled within ±5% variation of a standard value depending on the size of the tablet. The thickness

of the tablet was the only dimensional variable related to the tablet compression process.

Friability Test: Friability was the loss of weight of tablet in the container due to removal of fine particles from the tablet surface. Friability test was carried out to assess the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator was employed for finding the friability of the tablets. 10 tablets were taken and weighed from each batch and placed in Roche friabilator and allowed to rotate at 25 rpm for 4 minutes.

Dedust all the tablets and final weight was taken. The percentage of friability was calculated by using the following formula-

$$\% \text{ Friability} = (W1-W2) \times 100 / W1$$

Where, W1= Initial weight of tablets, W2 = Final weight of tablet.

Disintegration Test: The USP disintegration apparatus contains six glass tubes that are 3- inch long, open at the top and held against 10# screen at the bottom end of the basket rack assembly. One tablet was placed in each tube with one glass bid above each tablet in each tube and the basket rack was positioned in 1 Liter beaker filled with 900ml distilled water at 37 ±2°C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

Dispersion Test: Keep two tablets in 100ml water and stir gently for 2 minutes. The dispersion passed through 22#mesh. The tablets will consider passing the test if no residue remained on the screen.

Wetting Time: Place the five circular tissue papers of 10 cm diameter in a Petri dish containing 0.2% w/v methylene blue solution (3ml). A tablet was carefully placed on the surface of the tissue paper. The time required for developing blue colour on the upper surface of the tablet was noted as the wetting time.

Water Absorption Ratio: A small piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. Put tablet on the paper and the time required for complete wetting is measured. The wetted tablet was then reweighed. Water absorption ratio, R was determined by using following formula

$$R= Wa-Wb \times 100 / Wb$$

Where, Wa = The weight of tablet after water absorption, Wb = The weight of tablet before water absorption.

TABLE 4: POST COMPRESSION EVALUATION OF VENLAFAXINE HYDROCHLORIDE TABLET

Batch	Weight Variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	% Friability	Disintegration Time (sec)	Water Absorption Ratio	Wetting Time (sec)	*In-vitro* Dispersion Time (sec)
B1	240±0.04	7.96±0.08	3.13±0.03	0.84±0.08	51±0.04	80.6±0.03	32±0.05	42±0.05
B2	250±0.07	8.00±0.06	4.06±0.07	0.90±0.09	53±0.06	79.6±0.06	30±0.05	38±0.08
B3	260±0.08	7.92±0.04	3.90±0.02	0.79±0.06	43±0.07	81.1±0.02	35±0.08	40±0.04
B4	240±0.02	7.98±0.03	4.08±0.05	0.81±0.03	44±0.08	79.3±0.05	31±0.05	38±0.07
B5	260±0.01	7.96±0.01	4.03±0.01	0.81±0.06	46±0.08	75.7±0.08	36±0.06	43±0.03
B6	250±0.04	8.00±0.06	3.21±0.06	0.40±0.07	41±0.09	83.6±0.03	32±0.05	39±0.07
B7	250±0.09	7.93±0.03	3.87±0.04	0.82±0.08	47±0.04	78.6±0.08	30±0.02	39±0.08
B8	240±0.08	8.00±0.01	4.09±0.02	0.41±0.09	42±0.07	76.9±0.04	37±0.05	43±0.02
B9	250±0.01	7.90±0.02	4.11±0.07	0.81±0.02	47±0.03	81.9±0.03	30±0.06	37±0.04
B10	250±0.02	7.97±0.04	3.97±0.06	0.80±0.06	46±0.06	78.1±0.07	28±0.08	35±0.06
B11	250±0.04	7.91±0.05	4.03±0.04	0.42±0.04	43±0.05	78.3±0.08	22±0.04	32±0.09
B12	260±0.06	8.00±0.06	3.16±0.06	0.81±0.08	45±0.03	73.5±0.09	35±0.03	39±0.01

Each value represents the mean ± standard deviation (n=3).

***In-vitro* Dissolution Test:** *In-vitro* dissolution study was performed by using USP Type-II Apparatus (Paddle type) at 50 rpm. 900ml volume of Phosphate buffer pH 6.8 was used as dissolution medium which maintained at 37±0.5°C. Individual tablets of each batch were placed in the dissolution basket containing Phosphate Buffer pH 6.8 as a dissolution medium. The sample (1.0 ml aliquots) was collected at a regular time interval. The study was conducted for 60 minutes. The withdrawn

samples were transferred into a 10 ml volumetric flask and diluted to 10 ml by using phosphate buffer pH 6.8. The diluted Samples were analyzed for drug release by UV visible spectrophotometer at 225 nm [25-27].

TABLE 5: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING CROSPOVIDONE

Sr. no.	Time (min)	% Cumulative Drug Release of Venlafaxine HCl Containing Crospovidone		
		B1	B2	B3
1	0	0	0	0
2	5	41.11%±0.08	45.61%±0.05	46.63%±0.04
3	10	50.97%±0.07	53.23%±0.03	52.00%±0.06
4	20	61.46%±0.01	57.17%±0.04	58.81%±0.07
5	30	67.87%±0.01	64.19%±0.02	67.06%±0.09
6	45	71.83%±0.03	72.44%±0.04	75.72%±0.09
7	60	80.71%±0.02	82.14%±0.07	86.24%±0.06

Each value represents the mean ± standard deviation (n=3).

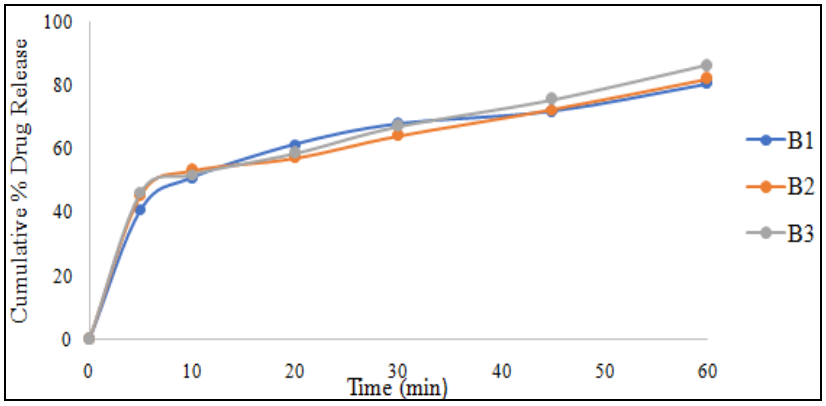

FIG. 2: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING CROSPOVIDONE

TABLE 6: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING SODIUM STARCH GLYCOLATE

Sr. no.	Time (min)	% Cumulative Drug Release of Venlafaxine HCl Containing Sodium Starch Glycolate		
		B4	B5	B6
1	0	0	0	0
2	5	40.09%±0.07	43.36%±0.04	50.11%±0.01
3	10	52.81%±0.03	57.32%±0.02	61.21%±0.07
4	20	60.44%±0.08	62.70%±0.06	66.60%±0.08
5	30	64.19%±0.02	68.29%±0.07	78.53%±0.03
6	45	74.90%±0.01	78.18%±0.03	82.51%±0.04
7	60	81.73%±0.05	85.84%±0.08	87.71%±0.06

Each value represents the mean + standard deviation (n=3).

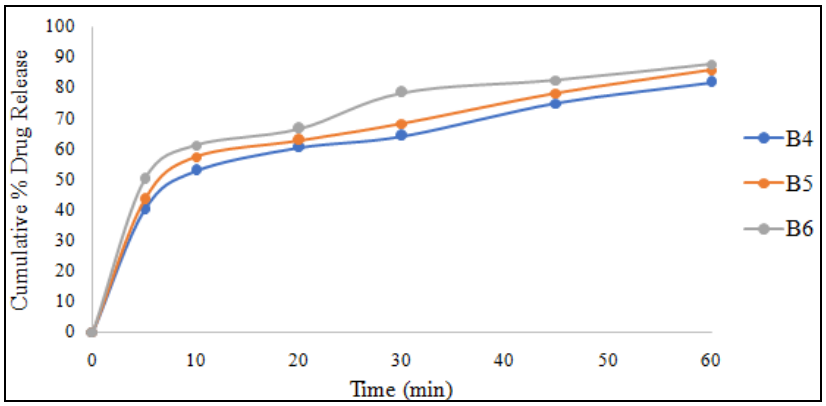

FIG. 3: % CUMULATIVE DRUGRELEASE OF VENLAFAXINE HCL CONTAINING SODIUM STARCH GLYCOLATE

TABLE 7: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING ISOMALT AND CROSPOVIDONE

Sr. no.	Time (min)	% Cumulative Drug Release of Venlafaxine HCl containing Isomalt and Crospovidone		
		B7	B8	B9
1	0	0	0	0
2	5	20.04%±0.09	23.11%±0.06	28.63%±0.02
3	10	22.31%±0.02	34.18%±0.03	32.55%±0.05
4	20	36.04%±0.08	40.15%±0.06	40.56%±0.06
5	30	42.63%±0.07	48.79%±0.05	53.70%±0.01
6	45	59.24%±0.06	61.32%±0.05	60.92%±0.03
7	60	64.42%±0.07	72.84%±0.06	74.28%±0.02

Each value represents the mean + standard deviation (n=3).

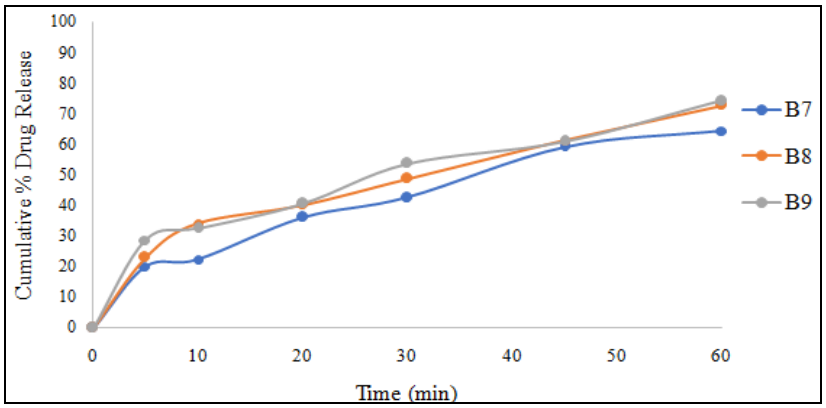

FIG. 4: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING ISOMALT AND CROSPOVIDONE

TABLE 8: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING ISOMALT AND SODIUM STARCH GLYCOLATE

Sr. no.	Time (min)	% Cumulative Drug Release of Venlafaxine HCl Containing Isomalt and Sodium Starch Glycolate		
		B10	B11	B12
1	0	0	0	0
2	5	33.13%±0.03	38.04%±0.08	36.00%±0.06
3	10	40.74%±0.08	41.36%±0.06	41.35%±0.03
4	20	49.37%± 0.06	48.15%±0.03	48.15%±0.06
5	30	55.36%±0.07	51.89%±0.08	51.88%±0.05
6	45	63.81%±0.05	61.35%±0.06	61.35%±0.05
7	60	72.47%±0.09	77.78%±0.03	75.74%±0.09

Each value represents the mean ± standard deviation (n=3).

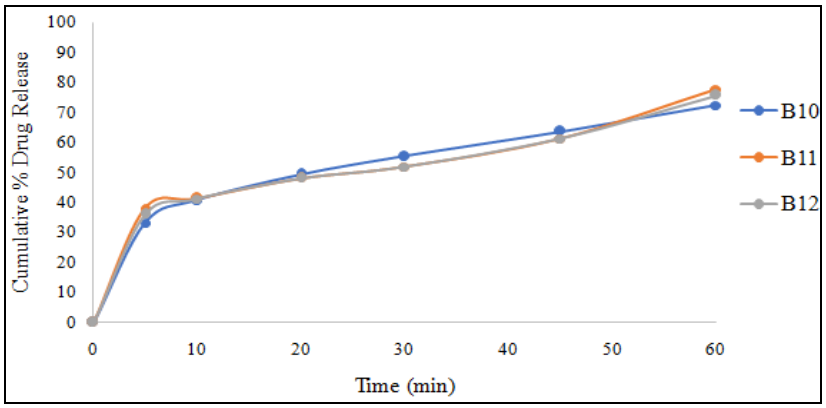

FIG. 5: % CUMULATIVE DRUG RELEASE OF VENLAFAXINE HCL CONTAINING ISOMALT AND SODIUM STARCH GLYCOLATE

RESULTS AND DISCUSSION: In present research work, an attempt was made to develop Oro-dispersible tablets containing Venlafaxine hydrochloride. The standard calibration curve of

Venlafaxine hydrochloride was prepared and constructed in Phosphate buffer pH 6.8 in 1-10µg/ml concentration and absorbance was taken on UV visible spectrophotometer at λmax 225nm. From the **Fig. 1**, it was observed that the plot was found to be linear, passed through origin and it was concluded that the curve follows the Beer Lambert's Law and correlation coefficient value was determined. Solubility of drug Venlafaxine hydrochloride was determined by solubilizing it in water and Phosphate buffer pH 6.8. The solubility of drug in water and phosphate buffer 6.8 should not be more than one. From the **Table 2,** it was observed that the solubility of drug in water was 9.84µg/ml ±0.07, and in phosphate buffer pH 6.8 was 9.35µg/ml±0.02. Thus, it was concluded that the drug Venlafaxine hydrochloride was freely soluble in both water and phosphate buffer.

A blend of powder was made using drug Venlafaxine hydrochloride, Avicel as directly compressible excipient, Talc and Magnesium Stearate as lubricant, Sodium Saccharine and Mannitol as sweetening agent, Isomalt as multifunctioning excipient and flavoring agent and different super disintegrating agents. Three batches (B1, B2, B3) were made using 25mg, 35mg and 45mg of Crospovidone with Avicel as directly compressible excipient. Similarly, three batches (B4, B5, B6) were made with 25mg, 35mg and 45 mg of Sodium Starch Glycolate with Avicel as directly compressible excipient as shown in **Table 1**. From **Table 3**, it was observed that for all the six batches (B1 to B6) angle of repose was found to be in the range 28.46°-36.10°, % compressibility index was found to be in the range of 11.47-30.08% and Hausner's ratio was found in between 1.12-1.43.

Likewise, six more batches (B7 to B12) were made with same quantities 25mg, 35mg and 45mg of Crospovidone and Sodium Starch Glycolate in combination with Isomalt as a multifunctioning agent by replacing other excipients as shown in **Table 1**. The blend of powder was evaluated using pre-compression parameters as specified. From the **Table 3** it was observed that angle of repose was found to be in the range of 25.17^{o}-34.16^{o}, % compressibility index was in the range of 13.97 – 22.33 and Hausner's ratio was in the range of 1.16 – 1.28.

Thus, it was concluded that the characteristics of powder blend for all the Batches (B1 to B12) containing Crospovidone and Sodium Starch Glycolate in combination with Avicel and Isomalt respectively were passed the all-pre-compression evaluation parameters showing good free- flowing properties. The direct compression method was adopted to formulate tablets by using Single Punch Tablet Machine. The compressed Oro-dispersible tablets were then subjected to post-compression evaluation. From **Table 4**, it was observed that the tablets exhibited weight variation was in between 240-260 mg, hardness was in between 3.13– 4.11 Kg/cm^2, % friability being in between 0.40-0.90%, disintegration time was in between 41-53sec, water absorption ratio was in between 73.5 – 83.6, wetting time was in between 22-37 sec and dispersion time being in between 32 to 43 sec. Due to less hardness, dispersion and disintegration time, the tablets were observed to disperse rapidly in the medium. Therefore, it was concluded that tablets from all batches passed all the post- compression evaluation parameters. The *in-vitro* dissolution test was carried out by using USP Type-II Paddle type apparatus to find out the % drug release for each tablet from Batch B1 to B12 in dissolution medium.

Phosphate buffer pH 6.8 from **Table 5** and **Fig. 2**, it was observed that Batch B1, B2 and B3 containing Crospovidone alone as super disintegrating agent showed 80.71%, 82.14% and 86.24% drug release in 60 min respectively. Whereas from **Table 7** and **Fig. 4**, it was observed that Batch B7, B8 and B9 containing combination of Isomalt and Crospovidone showed 64.42%, 72.84% and 74.28% drug release respectively in 60 min.

From **Table 6** and **Fig. 3**, it was observed that the Batch B4, B5 and B6 containing Sodium Starch Glycolate alone as super-disintegrating agent showed drug release of 81.73%, 85.84% and -87.71% drug release respectively in 60 min. On the contrary, from **Table 8** and **Fig. 5,** it was observed that Batch B10, B11 and B12 containing combination of Isomalt and Sodium Starch Glycolate showed lesser drug release 72.47%, 77.78% and 75.74% drug release respectively in 60 min. Hence from **Table 6** and **Fig. 3**, it was observed that Batch B6 containing 45 mg of

Sodium Starch Glycol ate showed maximum cumulative % drug release i.e., 87.71% in 60 min. Batch B6 also showed Weight Variation 250 mg, Hardness 3.21 Kg/cm^2, Friability 0.40%, Disintegration Time 41 sec, Water Absorption Ratio 83.6, Wetting Time 32 sec and *in-vitro* Dispersion Time 39 sec. Thus, based on the evaluation parameters, it was concluded that Batch B6 was the optimum batch among all batches in terms of bioavailability, optimum drug release and rapid onset of action. The result demonstrated effective use of Oro-dispersible tablets of Venlafaxine hydrochloride as an ideal drug release formulation for treatment of anxiety disorders or hypertension.

CONCLUSION: Orally dispersible tablets containing 25mg Venlafaxine hydrochloride drug were formulated using a combination of excipients. The tablets were formulated using a direct compression method, using a single punch machine. The formulated tablets were evaluated using pre and post- compression parameters. The Batch B6 showed optimum drug release of 87.71% in 60 min containing 45mg of Sodium Starch Glycolate as super-disintegrating agent.

The dispersion was found to be 39 seconds which is ideal as they should disperse in under a minute. Thus, Batch B6 was observed to show the desirable characteristics and considered to be the preferred dosage form for treatment of depression, anxiety and hypertension.

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