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Original Article

Invitro comparative study of venlafaxine HCl 75 mg capsules (extended released) available in the urban Karachi, Pakistan

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ABSTRACT

The In vitro drug release test of venlafaxine HCl 75 mg pellets capsule extended released available in Karachi Pakistan was the main aim of our study. Venlafaxine hydrochloride extended-release capsules for oral administration contain a novel antidepressant venlafaxine hydrochloride for the management of major depressive disorder Venlafaxine hydrochloride extended-release capsules is indicated. The evaluation test contain weight variation test, disintegration test and dissolution test(drug released test for 2 hours ,4 hours, 8 hours 12 hours and 20 hours) in specific dissolution medium demonstrated in pharmacopeia. All test results were comes out in a limits described in pharmacopeia.

Key Words: Venlafaxine HCl, pellets, extended release, antidepresent drug release, invitro study.

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INTRODUCTION

To optimize drug efficacy and reduce adverse effects and constant/sustained drug output with the objective of minimizing drug concentrations in the body the drug delivery systems have focused on these points. improved patient compliance and Reduced dosing frequency can also be expected for constant/sustained release drug delivery systems, compared to immediate release preparations(1) The active component in extended release compositions comprising as venlafaxine hydrochloride. The antidepressant Venlafaxine hydrochloride is an having formula (1)

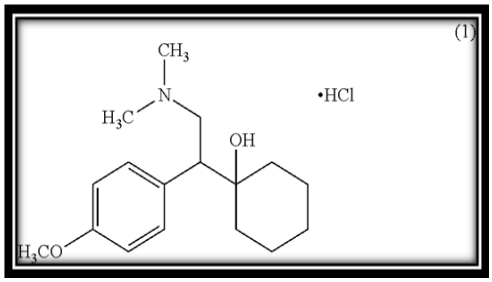

Figure 1: Structure of venlafexine HCl

Tablet and capsule sustained release formulations, are provided with a coating in the pharmaceutical formulation various coating techniques have been utilized to control the rate or the site of the release of the active (2) Venlafaxine hydrochloride is being selected (R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)-ethyl]cyclohexanol hydrochloride, the empirical formula is C17H27NO2 hydrochloride and 313.87 molecular weight. The solubility of venlafaxine is 572 mg/ml in water (adjustment to ionic strength of 0.2 M with sodium chloride). The appearance is white to off-white crystalline solid. Hydrogels are the rate-controlling polymers. Polymers such as hydroxypropylcellulose or ethyl cellulose are the examples of Cellulose ethers. [3] In relieving pain, Venlafaxine ER appears effective and safe (4). Venlafaxine hydrochloride (VenHCl) used in thermal microscopy and identified by variable-temperature powder X-ray diffraction at 180−190 °C.(5), Venlafaxine has a mechanism of action not related to other existing antidepressants due to its novel structure, commonly available examples of not related antidepressant are the imipramine, amitryptyline, trimipramine ,doxepin ,desipramine, nostriptyline, and protriptyline (6). With venlafaxine hydrochloride equivalent to 75 mg of venlafaxine base sustained release capsules of venlafaxine to be taken once daily. Appearance, weight variation, drug content and in vitro drug release are different physicochemical parameters. [7] Capsules usually containing water-soluble shell of suitable form of gelatin and within it one dose of drug enclosed. Capsules are solid doses. Within a hard capsule solid substances are enclosed where as liquids and semisolids are suitable for soft capsules. Dry-filled capsules are referred as Hard Gelatin Capsules .They consist of two sections namely the body & caps. By a mixture of water gelatin, water; sugar, with/ without suitable colouring agents a hard gelatin capsule can made. Evaluation of capsule contain Uniformity of weight, Content of active ingredient in capsule, Disintegration, Dissolution[8] Under the experimental conditions this test is provided to determine disintegration time when placed tablet or capsules in a liquid medium. For the peak spectral absorption of the substance Spectrophotometric assays are usually carried out. Small variations in the apparent wavelength of the peak may observed by different spectrophotometer, provided the two wavelengths do not differ by greater than ± 0.5 nm in the 240-280 nm range, by greater than ± 1 nm in the 280-320 nm range, and by greater than ± 2 nm above 320 nm, recalibration of the instrument may be indicated, if the difference is greater (9-10)

MATERIAL AND METHODS

Instruments: The instruments used for analysis of all four brands of 75 mg venlafaxine hydrochloride capsule, Electronic balance FX 400, Disintegration tester 121-L Galvano scientific,GDT-7L Galvano scientific dissolution testing apparatus, and spectrophotometer (UV – Visible) Shimadzu.

Methodlogy: Jinnah University for women Karachi Pakistan provided the opportunity to perform the pharmacopeal test included weight variation test, disintegration time test, assay and drug release test of four brands of venlafaxine HCl available in Karachi. All brands were purchased from different pharmacies available in Karachi description of the brands is expressed in table 2.

TEST METHODS

Uniformity of mass for single dose preparations: USP-32 described a weight test as a specified number of capsules which are weigh individually and the average weight is calculated and it should be within ±10%. For soft gelatin capsules, wash the shell with ether or some other suitable solvent. Individually weigh the emptied shells, the net mass of its contents should be calculated by subtracting the mass of the shell from the gross mass. The average net content determined from the sum of the individual net masses. The individual net content and the average net content should be determined by calculating the difference between the two weights.

Disintegration Time: The disintegration time of capsule or tablets was carried out by using disintegration apparatus .the disintegration tester

consist of a basket rack holding 6 tubes, open at the top and bottom. tablets and capsules that are not more than 18 mm use apparatus A . Use apparatus B for larger tablets and place one dosage unit in each of the six tubes of the basket and if specified add a disc. By using water as the immersion fluid unless another liquid is specified and maintain its temperature at 35–39 °C now operate the apparatus. At the end of the precise time lift the basket from the fluid and observe the dosage units, according to the USP -32 If one or two dosage units fail to disintegrate repeat the test on 12 additional dosage units. If not less than 16 of the 18 dosage units are disintegrated the requirements of the test are met

Assay (UV METHOD): The comparison of the absorbance produced by the solution of the test substance was done by UV-VIS spectrophotometer as described in the monograph with the absorbance of a solution of a reference substance.

***Standard Preparation*:** Weighed accurately 0.0500 gm of Venlafaxine HCl standard and transferred it into 100 ml volumetric flask. Added about 50 ml distilled water and shake to dissolved. Maked up the volume by using distilled water. Pipette 2 ml of this sample into volumetric flask of 100 mililiter volumetric flask and maked up the volume with distilled water and mixed well.

***Sample Preparation*:** Determined the average weight of 20 capsules, and now crushed the pellets into fine powder and weighed equivalent to Venlafaxine HCl standard and transferred it into 100 ml volumetric flask. Added 50ml of distilled water and shaked it for 30 minutes. After 30 minutes, maked up the volume with distilled water and shake well. Filter the above solution through Whatman # 1 filter paper. Dilute 2 ml of the above clear filtrate into 100 ml volumetric flask and maked up the volume by using distilled water and finally mixed well.

Measured the absorbance of both standard and sample preparation on a suitable spectrophotometer at 226 nm using distilled water as a blank.

Dissolution Test: Dissolution tester GDT-7L Galvano scientific used for the comparative study of venlafaxine HCl 75 mg capsules. Capsule drug release test was a standardized method used for measuring the rate of drug release from a dosage form. The principle function of the drug release test is to optimization of therapeutic effectiveness during product development and stability of different products lots.

Table 1: Conditions For Dissolution Test

Apparatus	USP Apparatus # 1 (Basket)
RPM	100
Medium	900 ml Distilled water
Temperature	37 ºC ± 0.5º C

Standard Preparation: Accurately weighed 0.1000 gm of Venlafaxine HCl standard and transferred it into volumetric flask of 100 mililiter. Added about 50 ml distilled water and shake to dissolved. Maked up the volume with distilled water. Pipette 2 ml of this solution into 100 mililiter volumetric flask and maked up the volume with distilled water and mixed well.

Sample Preparation: Accurately weighed 240 mg pellets and transferred to each dissolution vessel and operate the dissolution apparatus as per above mentioned condition, After 2, 4, 8 hrs 12 hrs and 20 hrs. withdraw the sample from the vessels and filtered through whatman # 1 filter paper. Prepared the dilution of sample same as standard, measured the absorbance of both standard and sample preparation on a suitable spectrophotometer at 226 nm, USP test 2 using water as a blank.

RESULTS

The comparative study of Venlafaxine HCl 75 mg capsule extended release showing results within the limits following USP. Physicochemical analysis of three different brands of Venlafaxine H Cl 75 mg capsule(XR) follow the weight variation test, disintegration test , dissolution on multi point and assay. Results of weight variation/average weight for Ven-01 was 242.7mg with (260.9025 – 224.5975mg) upper and lower limits, for Ven -2 average weight was 241 mg with (259.075– 222.925mg) upper and lower limits, for Ven -3 average weight was 164.5 mg with(176.8375-152.1625mg) upper and lower limits shown for Ven -4average weight was 222.6 mg with (239.295-205.905mg) upper and lower limits shown in table 02.The disintegration test showing results for Ven – 01 was 3 minutes,Ven-02 was 4 minutes,Ven – 03 was 4 minutes Ven – 04 was 3 minutes with the BP/USP limit(NMT 15 minutes) shown in table 05, The Dissolution test for sutained release capsule showing the results within the limits. Results for Ven– 01 is 94.24 %, Ven– 02 was 93.41 %, Ven – 03 was 91.24% , Ven-04 was 91.57% with USP limit NLT 80% shown in table 6,7 The results for Assay percent test for Ven-01 was 104.79 % ,Ven-02 was 100.09 % ,Ven -03 was 102.99% , Ven -04 was 102.68% with USP limit (90 – 110 %) shown in table 8 & 9.

DISCUSSION

It is compulsory to make sure that drug dissolution occurs whenever a new solid dosage form is developed or produced, The registration authorities and the pharmaceutical industries do focus on dissolution studies of drug. The quantitative analysis and numerical formulas of the dissolution/release tests is easier and used for the

calculation of the results[10] .To evaluate and compare the effectiveness of the four different brands of Venlafaxine HCl 75 mg capsule(XR) available in local market was the main objective of this research work, according to the USP evaluation of physical and chemical test like weight variation test , disintegration ,dissolution and assay percent test showing results within their limits. Results of weight variation test were within specified upper and lower limit of 7.5%, All brands of Venlafaxine HCl 75 mg capsule(XR) showed disintegration time within the limits, according to USP the capsule should not take more than 15 minutes to dissolved the capsule results by evaluating this comparision the Ven-01 and Ven - 04 capsule dissolve within 3 minutes as measured up to the other marketed brands which took 4 minutes to dissolve.US Pharmacopeal limits of dissolution test is NLT 80 % in 20 hours and all four brands of Venlafaxine HCl 75 mg capsule(XR) dissolved within time and Ven – 01 showed excellent results as compare to other brands, according to the USP the Venlafaxine HCl 75 mg capsule(XR) have 90 – 110% limit of assay percentage by comparing four brands of Venlafaxine HCl 75 mg capsule(XR) all brands showed results within the acceptable limits.

CONCLUSION

It is concluded from all results of all four brands of Venlafaxine HCl 75 mg capsule(XR) that all brands reveals minor variation in their results but these variation comes under the specified limits, so quality standards of all four brands are same but there is a difference in their packaging and there MRP's.

Table 2: General Table

Brand Name	Serial number	Code Number	Batch number
Efexor	Ven-1	023658	L59493
Venice	Ven--2	032269	011
Venalax	Ven--3	040955	T 1626
SnRI	Ven--3	055878	14S101

Table 3: Statistical Uniformity of mass for unit dose preparation

Serial number	Batch number	Average weight (x) mg U.S.P	Standard deviation (S)	Upper Limit U.S.P (UCL=X+ 7.5 S)	Lower Limit U.S.P (LCL=X+-7.5 S)
Ven-1	L59493	242.7	0.9486	260.9025	224.4975
Ven—2	011	241	2.867	259.075	222.925
Ven—3	T 1626	164.5	1.394	176.8375	152.1625
Ven—4	14S101	222.6	1.985	239.295	205.905

Table 4: Disintegration Test

Serial number	Code Number	Batch number	Disintegration Time Result (%)	B.P/USP Spec.	Deviation From BP/USP
Ven-1	023658	L59493	3min	NMT 15 min	Pass
Ven—2	032269	011	4 min	NMT 15 min	Pass
Ven—3	040955	T 1626	4min	NMT 15 min	Pass
Ven—4	055878	14S101	3min	NMT 15 min	Pass

Table 5: Dissolution Test

5.1 Absorbance of Standard

Serial number	Absorbance
Ven—Standard	0.560

5.2 Absorbance of Samples

Serial No.	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance
	0 min	2 hour	4 hour	8 hour	12 hour	20hour
Ven-1	0.057	0.165	0.284	0.422	0.505	0.565
Ven—2	0.046	0.115	0.280	0.420	0.483	0.560
Ven—3	0.048	0.169	0.283	0.361	0.466	0.547
Ven—4	0.019	0.166	0.315	0.400	0.486	0.549

Table 6: Dissolution Test(10)

Serial number	Code Number	Batch number	Dissolution test Result(%)					USP Spec.					Deviation From Official limit
			2h	4h	8h	12h	20h	2h	4h	8h	12h	20 h	
Ven-1	023658	L59493	27.52	47.3	70.3	84.22	94.2	10-30%	33-53%	58-78%	68-88%	NLT 80%	Pass
Ven-2	032269	011	19.18	46.70	70.05	80.56	93.41						Pass
Ven--3	040955	T 1626	28.19	47.2	60.2	77.73	91.2						
Ven-4	055878	14S101	27.69	52.5	66.7	81.06	91.5						Pass

Table 7: Assay percent Test

Serial number	Absorbance
Ven—standard	0.576
Ven-1	0.592
Ven—2	0.582
Ven—3	0.859
Ven—4	0.623

Table 8: Assay percent Test

Serial number	Code Number	Batch number	Assay percent test Result (%)	USP Spec.	Deviation From Official limit
Ven-1	023658	L59493	104.79	90 -110%	Pass
Ven—2	032269	011	100.09	90 -110%	Pass
Ven—3	040955	T 1626	102.99	90 -110%	Pass
Ven—4	055878	14S101	102.68	90 -110%	Pass

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