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Comprehensive Review on Analytical Profile of Antidepressant Drug

Bhaskar Rajveer[1], Ola Monika[2], Patil Amod[3], Chaudhari Kamlesh[1], Ambatkar Ankita[1], Mahajan Tejaswini[1]

[1] Dept. of Quality Assurance, RCPIPER, Shirpur, INDIA, 425405

[2] Dept. of Pharmaceutics, RCPIPER, Shirpur, INDIA, 425405

[3] Dept. of Pharmaceutical Chemistry, RCPIPER, Shirpur, INDIA, 425405

ABSTRACT

Venlafaxine is an antidepressant belonging to a group of drugs called selective serotonin and norepinephrine reuptake inhibitors (SSNRIs). Venlafaxine affects chemicals in the brain that may be unbalanced in people with depression. It is used to treat major depressive disorder, anxiety and panic disorder. The present review assesses the various approaches for analysis of Venlafaxine in bulk drug as well as various formulations. A concise review represents the compilation and discussion of about more than 35 analytical methods which includes HPLC, HPTLC, UPLC, LC-MS and UV-Spectrophotometry methods implemented for investigation of Venlafaxine in biological matrices, bulk samples and in different dosage formulations. This detailed review will be of great help to the researcher who is working on Venlafaxine.

Keywords: Venlafaxine; Analytical Profile; HPLC; HPTLC; Bioanalytical; Stability indicating

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***Address for Correspondence:**

Kamlesh Chaudhari, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule (MS), India 425405,

Abbreviations:

VEN: Venlafaxine
API: Active pharmaceutical ingredients
pKa: Dissociation constant
Log P: Partition co-efficient
HPLC: High performance liquid chromatography
RP-HPLC: Reverse phase-high performance liquid chromatography
HPTLC: High performance thin layer chromatography
UPLC-MS: Ultra-performance liquid chromatography-mass spectrometry
UPLC-TMS: Ultra-performance liquid chromatography-tandem mass spectrometry
LC-MS: Liquid chromatography-mass spectrometry
PDA: Photodiode array
TLC: Thin layer chromatography
F254: Fluorescence indicator
ICH: International conference on harmonization
SIM: Stability indicating method

Introduction

Depression is excessive general and disabling disease with important social and economic outcome, most of anti-depressant agents are accessible in management of disorder, they are limitations of efficacy, because of toxic effects can be encountered. Most harmful effects found to risk for life threatening arrhythmias, particularly in patients with early survive cardiac disease or after overdose direction. Because depression and nervousness disorders are related with acute and prevalent psychosocial and occupational disfunction, significant reason of abnormality associated with chronic disease like, rheumatoid arthritis, hypertension and diabetes.[1]

It was referred to as a Serotonin nor-epinephrine dopamine reuptake inhibitor. Venlafaxine HCl was available in market name of Effexor tablets. [2]

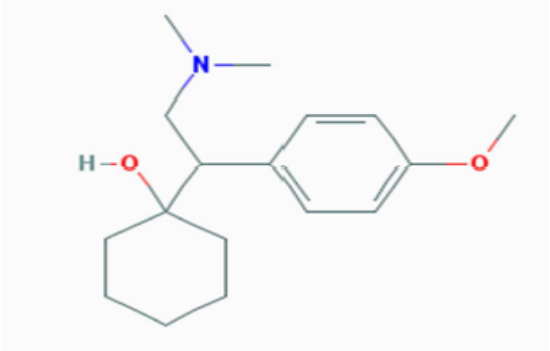

Figure 1. Structure of Venlafaxine HCl

In investigative examination endeavor originate a novel, reproducible and efficient HPLC technique with isocratic elution for assurance of venlafaxine in pharmaceutical formulations. These technique created was approved and utilized for the examination of venlafaxine HCl in cases and tablets.[3] Which are work in completed results of venlafaxine HCl our best information, venlafaxine isn't accessible in any pharmacopeia and no technique for assurance of pollutions has been singular strategies either in mass medications or pharmaceuticals, accordingly best potential for advancement of logical techniques to analyze the degrees of contaminations in completed results of venlafaxine during the procedure of improvement. [4]

Table no.1: Drug Profile of Venlafaxine HCl :

Drug Name	Venlafaxine HCl
Category	Anti-depressant
Chemical formula	$C_{17}H_{27}NO_2$
IUPAC Name	1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexane-1-ol
Molecular weight	277.402
Melting point	215-217
Solubility	Freely soluble: Water, Methanol
BCS Class	Class-I (High solubility and high permeability)
Half life	5 hours
pKa value	Strongestacid-14.42, Strongest base-8.91
log P value	LogP 2.69, LogP 2.74
log S value	-3.1
CAS No.	93413-69-5

Venlafaxine HCl side effects:

Common venlafaxine side effects may include:

- Mood or behavior changes
- Anxiety
- Panic attacks
- Trouble sleeping
- Feel impulsive, irritable, agitated, aggressive, restless
- Nausea, vomiting, diarrhea
- Dry mouth
- Dizziness, headache, feeling nervous
- Fast heartbeats, vision changes
- Decreased sex drive, or difficulty having an organism.

Serious side effects:

- Attempting suicide
- Acting on dangerous impulses
- Thoughts about suicide or dying
- New or worsened depression
- New or worsened anxiety or panic attacks

Therapeutic uses of Venlafaxine HCl:

- Treatment of diabetic neuropathy
- Effectiveness of migraine prophylaxis
- Treatment of prostate cancer
- Action on both serotoninergic and adrenergic systems
- Reduce episodes of cataplexy
- Improve patient mood and energy level
- Help restore patient interest in daily living.

Analytical techniques used for determination of Venlafaxine HCl:

A.High-performance liquid chromatography (HPLC):

HPLC is a propelled fluid chromatography utilized in isolating the combine blend of particles experienced in substance and organic structure. In year 1980, HPLC technique originate for first time examine of mass medications materials (USP,1980). The essential pieces of a HPLC are a solvent (A) Pump (B) Injector (C) Segment (D) Detector/Recorder. Each segments are associated in an arrangement to one another by steel tubing. The pump controls the progression of solvent through the system. Upon leaving the pump, solvent enters the injector, at that point goes through the section, lastly through the optical unit of a detector. [5] The partition of a compound includes its physical cooperation with a stationary stage and a portable stage. In HPLC the stationary stage is incredibly little. A standard molecule size for column chromatography is 60 microns, while that for HPLC is ordinarily 5 microns, or the size of a spot of residue solvent course through such thick material requires a high weight, so in HPLC the stationary stage is stuffed in a hardened steel cylinder, and solvent is pumped through the framework under high weight, as much as a few thousand pounds for every square inch. This weight brings about a stream pace of a few ml's per minute.[6] It broadly use detectors in HPLC is UV-detectors is equipped for inspect a few wavelengths is conceivable to applying the various wavelength in examining program. UV-detector surety all the UV-engage parts are identified.

The photodiode cluster (PDA) detector is likewise utilized in HPLC instrument. Most delicate detector among the LC detector is fluorescence detector. A photodiode cluster (PDA) is a lined exhibit of discrete photodiodes on a coordinated circuit (IC) chip for spectroscopy. It is put at the picture plane of a spectrometer to enable a scope of wavelengths to be detected simultaneously. [5]

Table no.2: HPLC method for venlafaxine HCl:

Sr. no.	Drug	Method	Stationary phase	Mobile phase	Detection	Linearity, LOD, LOQ (µg/mL)	R_t / F_R	Ref
1	Venlafaxine HCl	HPLC	C18(150×4.6mm, 5µm) Coupled to Guard column C18 (30×4.6mm, 5µm)	Acetonitrile, Potassium phosphate buffer (pH6.5) (30:20v/v)	228 nm UV-visible detection	Linearity: 1.05-10.5µg/mL LOD:-- LOQ: --	Rt:15.2 min Fr:1 mL/min	7
2	Venlafaxine HCl	RP-HPLC	ODS-C18 (50×4.6mm, 5µm)	Acetonitrile, Sodium acetate (65:35 v/v)	225 nm	Linearity: 2.0-50.0µg/mL LOD:-- LOQ: --	Rt:2.83 min Fr: 1 mL/min	8
3	Venlafaxine HCl	HPLC	ODS RP-C18 (4.6×150mm,5µm)	Acetonitrile, Water(70:30v/v)	230nm	Linearity: 9 µg – 2 µg/mL LOD:1.3µg/mL LOQ:1.10 µg/mL	Rt: 4.8 min Fr: 1.5mL/min	9
4	Venlafaxine HCl	RP-HPLC	Microsorb MV 100 C18 (250×4.6mm,5µm)	Acetonitrile, 0.04 potassium dihydrogen phosphate, Methanol (45:25:30 v/v)	224 nm	Linearity: 1-50 µg/mL LOD: 0.568µg/mL LOQ: 1.72 µg/mL	Rt:3.43 min Fr:1 mL/min	3
5	Venlafaxine HCl , Modafinil	RP-HPLC	C18 (4.6×250mm,5µm)	Ammonium acetate buffer (pH4.0), 10% Methanol in acetonitrile (60:40)	225 nm	Linearity: 1.0-50 µg/mL LOD: -- LOQ: --	Rt: Venlafaxine 4.4min Modafinil- 6.4 min Fr:1mL/min	10
6	Venlafaxine HCl	HPLC-MS/MS	Varomycin chiral column (250×4.6mm,5µm)	Methanol, Ammonium acetate(8:92 v/v)	224 nm	Linearity: 0.28-423.0 µg/mL LOD:0.02 µg/mL LOQ:0.28 µg/mL	Rt: 6.72 min Fr: 1 mL/min	11
7	Esomeprazole, Venlafaxine HCl Fenofibrate	HPLC	C18 (150×4.6mm, 3.5µm)	A-Acetonitrile, buffer(25:75v/v) B-Acetonitrile, buffer(30:70v/v)	230 nm	Linearity: 10.37-518.40µg/mL Esomeprazole LOD:1.02µg/mL LOQ: 5.18 µg/mL Venlafaxine HCl LOD:1.02µg/mL LOQ:5.09 µg/mL Fenofibrate LOD:1.05µg/mL LOQ:5.22 µg/mL	Esomeprazole Rt:3.25min Fr: 1.1 mL/min Venlafaxine HCl Rt:4.7min Fr:1.1 mL/min Fenofibrate Rt:13.12min Fr: 1.1mL/min	12
8	Venlafaxine HCl, o-desmethyl venlafaxine	HPLC	C18 (25×4.6mm)	Methanol, Acetonitrile (95:5v/v) and 40%Ammonium acetate	235 nm	Venlafaxine HCl Linearity range: 1-20µg/mL LOD:0.2µg/mL LOQ:0.5 µg/mL O-desmethyl Ven. HCl Linearity range: 1-25µg/mL LOD:0.3µg/mL LOQ:1.0µg/mL	Venlafaxine HCl Rt: 7.2 min Fr: 0.7mL/min. O-desmethyl Ven. HCl Rt:4.9min Fr: 0.7 mL/min	6
9	Venlafaxine HCl	RP-HPLC	Kromasil KR100-5 C18(4.6×250mm, 5µm)	Diethylamine buffer, Methanol (90:10 v/v)	225nm PDA detection	Linearity: 0.5-5.0µg/mL LOD:0.095µg/mL LOQ: 0.29 µg/mL	Rt: 5 min Fr:1mL/min	13
10	Venlafaxine HCl	RP-HPLC	C18Isocratic column(250×4.6mm, 5µm)	Acetonitrile, Water(50:50v/v)	226 nm	Linearity: 1-5µg/mL LOD:0.0665µg/mL LOQ:0.199 µg/mL	Rt: 3.5 min Fr: 1.0mL/min	14

B. UV- visible spectrophotometric method:

UV-visible spectroscopy is examining the wavelength of typical sample. The UV-visible spectra have expensive highlights are restricted use for test identification are helpful for quantitative estimations. Spectrophotometric method is most significant technique is recognize the substance element on premise of transmission or reflection properties of material as capacity of wavelength, adheres to the Beer-Lambert's law and synthetic compound which bear a chromophoric bunch for retention of light, it consume the less time when contrasted with other technique and gives incredible accuracy in practical.[15] The writing overview educate the UV techniques and RP-HPLC strategy are accounted for the assurance of venlafaxine HCl exclusively with different medications present examination includes improvement and approval of new UV-spectroscopy technique for assurance of venlafaxine HCl in unadulterated and its pharmaceutical plans suggest economical conditions. The investigative strategy was approved by ICH guidelines approval parameters. [16]

Distilled water was researched to build up a reasonable UV-visible spectrophotometric technique for the investigation of Venlafaxine hydrochloride in details. For choice of media the criteria utilized were affectability of the technique, simplicity of test planning, dissolvability of the medication, and cost of solvents and appropriateness of strategy to different purposes. [17]

Table no.3: UV- Spectrometric Method for Venlafaxine HCl :

Sr. No.	Drug	Matrix	Method	Solvent	Detection	Linearity/LOD, LOQ	Ref.
1	Venlafaxine HCl	Bulk and Formulation	UV-visible spectrophotometric method (JascoV-630)	0.1N NaOH	223 nm	Linearity: 5-25µg/mL R^2:0.996 LOD:0.95µg/mL LOQ: 0.29µg/mL	18
2	Venlafaxine HCl	Bulk and Formulation	Double beam perkin Elmer UV-visible spectrophotometer (Model Labda 25)	Water	225 nm	Linearity: 4-24µg/mL R^2:0.9991 LOD:-- LOQ: --	17
3	Venlafaxine HCl	API	ELICO SL-210 double beam UV-visible spectrophotometer	Water	225 nm	Linearity: 2-24µg/mL R^2:0.999 LOD:0.955µg/mL LOQ:2.895µg/mL	19
4	Venlafaxine HCl	Bulk and Formulation	UV-visible spectrophotometer model 117 with resolution of 0.1 nm	Phosphate buffer (pH6.8)	222 nm	Linearity: 2-26µg/mL R^2:0.9999 LOD:-- LOQ: --	20
5	Venlafaxine HCl	Capsule dosage form	UV 1601 series (Shimadzu), UV-visible double beam spectrophotometer	Water	274 nm	Linearity: 50-250µg/mL R^2:0.9998 LOD:-- LOQ: --	21
6	Venlafaxine HCl	Bulk and Tablet form	Systronics UV-visible spectrophotometer Model-2203	Water	626 nm	Linearity: 10-50µg/mL R^2:0.9995 LOD:-- LOQ:--	22
7	Venlafaxine HCl	Bulk and Formulation	UV- spectrometry	Water	225 nm	Linearity: 50-160µg/mL R^2:0.9995 LOD:0.29µg/mL LOQ:1.01µg/mL	23

C. High performance thin layer chromatography (HPTLC):

Planar Chromatography instead of column chromatography (for example GC, HPLC) uses a level (planar) stationary stage for detachment. In Thin-Layer Chromatography (TLC) this stationary stage is support by magnifier sheets or a foil (plastic or aluminum). Again dissimilar to section partitions, of TLC plate comprises an open framework, which goes entire individual strides of TLC investigation in a disconnected mode. HPTLC is a most adaptable strategy and is known for consistency, immaculateness profile, measure and exactness and precision of results. It can deal with a few examples of even dissimilar nature and structure. Synthetic

inspection is necessary section in enabling a research center to guarantee routine satisfying enforcement execution of scientific strategies. Arrangement and put resources into stages to a ultra-modern completely programmed HPTLC slope System with different identifiers. Perceivability of the example all through the chromatographic examination i.e., after example application and chromatograph advancement.[24] The HPTLC framework (Camag, Muttenz, Switzerland) furnished with an example implement Linomat-V associated with a nitrogen chamber, twin trough plate advancement chamber (10×10cm), TLC Camag Scanner III and Wincats-4.02 pre-covered silica gel 60 F254 TLC aluminum plates.[25] Most labs use TLC/HPTLC for investigation, test, or examination with comparable examples, screening of unclear examples or large number of samples. Quality control, logical R&D, process observing, and ecological labs discover TLC/HPTLC as a valuable instrument for standard investigation. [26]

Table no.4: HPTLC Method for Venlafaxine HCl :

Sr. no.	Drug and Matrix	Stationary phase	Mobile phase	Chamber saturation/ TLC plate development time	Detection	Linearity, LOD, LOQ (µg/mL)	Ref.
1	Venlafaxine HCl (Bulk, Capsule formulation)	Precoated Silica gel 60 F254 (10×10cm, 0.2mm Thickness) TLC plate	Methanol, Ammonia (4.5:0.5 v/v)	CSt: 25min PDt: 20min Rf value: 0.65	Densitometry scanning at 224nm	Linearity: 500-3000 µg/mL R^2: 0.998 LOD: 7.7µg/mL LOQ: 23.3µg/mL	25
2	Venlafaxine HCl (API and pharmaceutical dosage form)	Precoated Silica gel 60 F254 on Aluminium sheets (10×10cm, 0.2mm Thickness) TLC plate	Toluene, Methanol (4:6 v/v)	CSt: 25min PDt: 20min Rf value: 0.47	Densitometry scanning at 230nm	Linearity: 2-7µg/mL R^2: 0.996 LOD: 0.17µg/mL LOQ: 0.53µg/mL	27
3	Venlafaxine HCl (Bulk, Tablets)	(10×20cm) Aluminium backed HPTLC plates coated with 0.2mm layer of Silica gel 60 F254	Toluene, Methanol (7:3.5 v/v)	CSt: 10min PDt: 20min Rf value: 0.19	Densitometry scanning at 228nm	Linearity: 400-2000µg/mL R^2: 0.999 LOD: 97.12µg/mL LOQ: 294.30µg/mL	28

D. Stability indicating method:

Singh and Bakshi discussed some conclusive points of developing SIM. [29] Dolan suggests the comments on SIA. [30] Smela discussed regulatory points about SIM is analytical method.[31] SIM procedure is used to measure the diminution the quantity of API in drug substances prefer degradation studies. SIM may also check stability of drug matter and products changes in separate time intervals of study. These method accurately estimate the changes API concentrations in the absence of impurities, excipients and other degradation products.

Stress testing is done to demonstrate specificity of the created method to quantify the adjustments in grouping of substance when little data is accessible about prospective degradation product. The improvement of reasonable stability indicating method provides a background for preformulation thinks about, stability examines and improve the proper storage condition. [32]

These ICH guidelines are relevant to forced degradation study:

- ICH Q1 A: Stability testing of new drug substance and products.[33]
- ICH Q1 B: Photostability testing of new drug substance and products.[34]
- ICH Q2 B: Validation of analytical procedure, methodology.[35]

Solution state stability:

1. Acidic hydrolysis
2. Alkaline hydrolysis
3. Hydrolytic
4. Oxidative degradation

Solid state solubility:

1. Thermal degradation
2. Photolytic degradation

Table no.5: Stress Testing: (forced degradation) :

Degradation factor	Condition
Thermal	≥ 60^0C
Humidity	≥ 75% RH
Acid	0.1N HCL
Base	0.1N NaOH
Oxidative	Oxygen gas, 3% H_2O_2
Photolytic	Metal halide, Hg, Xe lamp, UV-B fluorescent

Table no.6: Stability indicating method for venlafaxine HCl:

Sr. No.	Method	Drug	R.T&R.T of Degradation Product/Development Time Rf value of drug	Column/ Stationary phase	Mobile Phase & Flow Rate, Chamber saturation time	Wavelength, Linearity, Coefficient correlation.	LOQ & LOD (µg/mL)	Ref
1	HPLC	Venlafaxine HCl (Extended release)	Run time- 15min Retention time- 4.49min	(5µm, 250×4.6mm) Kromacil C18 column	Phosphate buffer (pH4.5), Methanol (40:60) Flow rate- 1mL/min	UV-detection 225 nm Linear range- 42-78µg/mL R^2=0.9997	LOD- 0.075µg/mL LOQ- 0.15 µg/mL	36
2	HPLC	Venlafaxine HCl (Sustained release tablet)	Run time- 10min Retention time- 7.6min	(5µm, 250×4.6mm) RP inertsil ODS-3V C18 column	Phosphate buffer, Acetonitrile (80:20) Flow rate- 0.8ml/min	UV-detection 225 nm Linear range- 0.1-5 µg/mL R^2=0.9999	LOD- 0.26 µg/mL LOQ- 0.81µg/mL	37
3	LC	O-Desmethylvenlafaxine (API)	Run time- 14min Retention time- __	(3µm, 150×4.6mm) YMC-pack ODS-A column	A) Buffer, Acetonitrile (85:15 v/v) B) Water, Acetonitrile (20:80 v/v) Flow rate-1ml/min	230 nm Linear range-20-160 µg/mL R^2=0.9996	LOD- 0.04 µg/mL LOQ- 0.13 µg/mL	38
4	LC	Venlafaxine HCl	Run time- 10min Retention time- 4.32min	(5µm, 4.6×250mm) Spherisorb C8 column	Acetonitrile, Sodium dihydrogen orthophosphate(pH6.8) (75:25) Flow rate – 1.5ml/min	224 nm Linear range-1-10 µg/mL R^2=0.9999	LOD- 150 µg/mL LOQ- 600µg/mL	39
5	LC	Venlafaxine HCl (Extended release capsule)	Run time- 10min Retention time- 6.8min	(5µm, 250×4.6mm) luna C18 column	Phosphoric acid, Acetonitrile, Methanol (62:30:8) Flow rate- 1ml/min	226 nm PDA detector Linear range- 10-70µg/mL R^2=0.9999	LOD-0.24 µg/mL LOQ-0.80 µg/mL	40
6	HPTLC	Venlafaxine HCl (Bulk & dosage form)	TLC Pate Development time – 20min Rf value- 0.46±0.05	(10×10cm, 2mm thickness) Aluminium plates precoated silica gel 60 F254	Dichloromethane, Acetonitrile, N-Hexane, Triethylamine (0.5:0.5:4:0.7) Saturation time- 15min	Camag TLC scanner-3 225 nm Linear range-100-1000µg/mL R^2=0.9918	LOD- 12.48µg/mL LOQ- 37.81µg/mL	41
7	HPTLC	Venlafaxine HCl	TLC plate Development time- 25min Rf value- 0.58±0.02	(10×10cm, 2mm) HPTLC plate coated with 0.25mm layer of silica gel 60 F254 plates	Butanol, Acetic acid, Water (6:2:2) Saturation time- 20min	Reflectance scanning camag TLC scanner-3 225 nm Linear range-100-600µg/mL R^2=0.9984	LOD- 39.23µg/mL LOQ- 130.89µg/mL	42

E. Bio-analytical method:

These bioanalytical validation technique established by Karnes et al. in 1991which was intentional to give direction to bioanalytical chemists. After one year, Shah et al. established these report the convention on Analytical technique validation of bioavailability, bioequivalence and pharmacokinetic studies organized in Washington in 1990. [43]

Bio-analytical method promotes the quantitative analytical technique appropriate biochemical approach. HPLC, RP-HPLC, HPLC-MS/ESI, UPLC-MS, UPLC-TMS, LC and GC combined with mass spectroscopic procedure, LC-MS, LC-

MS/MS. Bioanalysis is innovative technique for improve the accuracy, precision, efficiency, sensitivity, specificity, assays, data handling, processes, analysis cost, data quality. [44]

Table no.7: Bioanalytical method for venlafaxine HCl :

Sr. No.	Method	Drug	Bio. Fluid	Column	Mobile Phase	Flow Rate & Retention Time	Detection/Detector	Linearity & LOD&LOQ	Ref.
1	RP-HPLC	Venlafaxine and O-desmethyl	Human Plasma	(4.6×150mm,5µm) Spherisorb S5 C18 column	Acetonitrile, Phosphate buffer (30:70v/v)	Flow rate-1.4mL/min Retention time-8min	UV-Detector and Datajet integrator at 229nm	Linearity: 0.2-0.5µg/mL LOD:-- LOQ: --	45
2	RP-HPLC	Venlafaxine HCl	Human Plasma	(150×4.6mm,5µm) Alltima C8 column	0.1% O-phosphoric acid, Methanol (50:50 v/v)	Flow rate-0.7mL/min Retention time-7min	___	Linearity: 2-25µg/mL LOD-2.00µg/mL LOQ-5.00µg/mL	27
3	HPLC-ESI/MS	Venlafaxine and O-desmethylvenlafaxine enantiomers	Human Plasma	(250×4.6mm,5µm) Vancomycin chiral column	Ammonium acetate, Methanol (15:85v/v)	Flow rate-1mL/min VEN Retention time-11.8min ODV Retention time-11.2min	Ionized in the positive electrospray ionization ion source of the mass spectroscopy	Linearity: - VEN: 5.0-400µg/mL LOD1.0µg/mL LOQ-5.0µg/mL ODV: 4.0-300µg/mL LOD-1.5µg/mL LOQ-4.3µg/mL	47
4	HPLC-MS/ESI	Venlafaxine and its three metabolites	Human Plasma	(250×4.6mm,5µm) Thermo BDS hypersil C18 column	Water, Acetonitrile (60:40 v/v)	Flow rate-1mL/min VEN Retention time-4.43min ODV Retention time-3.01 min NDV Retention time-3.95min DDV Retention time-2.88min	Ionized in electrospray ionization ion source of mass spectrometer detected in selected ion recording	VEN Linearity: 4.0-700µg/mL LOD-0.4µg/mL LOQ- 3.5µg/Ml ODV Linearity: 2.0-900µg/mL LOD-0.2µg/mL LOQ-2.2µg/mL NDV Linearity: 3.0-800µg/mL LOD-0.3µg/mL LOQ-2.7µg/mL DDV Linearity: 2.0-700µg/mL LOD-0.2µg/mL LOQ-1.9µg/mL	48
5	UPLC-TMS	Venlafaxine and O-desmethylvenlafaxine	Human Plasma	(50×2.1mm, 1.7µm) Acquity UPLCBEH C18 column	Methanol, Ammonium acetate (85:15 v/v)	Flow rate-0.30mL/min Retention time- 3 min	Triple quadrupole tandem mass spectrometer (TMS) via electrospray ionization source (ESI)	Linearity: 0.200-200µg/mL LOD-0.10µg/mL LOQ-0.200µg/mL	49

6	LC-MS/MS	Venlafaxine and O-desmethylvenlafaxine	Rat Plasma	(150×4.6mm,5µm) Water symmetry C18 column	Ammonium formate, Methanol (20:80 v/v)	Flow rate-0.8mL/min Retention time-2.3min	Scanning range at 0-300 amu	Linearity: 10-8000µg/mL VEN LOD-3.35µg/mL LOQ-10.10µg/mL ODV LOD-3.86µg/mL LOQ-10.10µg/mL	50
7	HPLC	Venlafaxine and O-desmethylvenlafaxine	Human Saliva	(150×4.6mm,UGA-120A 5µm)C18 column(5×4mm) C18 Guard column	Acetonitrile, Water (50:50 v/v)	Flow rate-1 mL/min Retention time-12.3min	226 nm	Linearity: 1-1000µg/mL VEN LOD-3.1µg/mL LOQ-0.2µg/mL ODV LOD-2.8µg/mL LOQ-9.4µg/mL	51
8	UPLC-MS	Venlafaxine and O-desmethylvenlafaxine	Rat Plasma	(100×2.1mm,1.7µm) AcquityUPLCBEH shield RP18 column	Water, Acetonitrile (20:80 v/v)	Flow rate-0.3mL/min VEN Retention time-0.93min ODV Retention time-0.83min	Ionized in electrospray ionization ion source of mass spectrometer	Linearity: 10-2000µg/mL VEN LOD-2.66µg/mL LOQ-7.98µg/mL ODV LOD-2.78µg/mL LOQ-8.34µg/mL	41

Conclusion

The present review illustrates various analytical approaches exercised for the estimation of Venlafaxine. A numerous investigation had perform including, Bio-analytical, Stability indicating, HPLC, HPTLC, UV-Visible Spectroscopy, and LC-MS, etc. for estimation of Venlafaxine in bulk and in its combined pharmaceutical formulations and in plasma. Liquid chromatography with UV detection has been found to be most studied for estimation of ven. in bulk as well as pharmaceutical dosage forms, while hyphenated such as LC-MS methods are reported for determination of Venlafaxine and its metabolite in plasma and other biological fluids. Few chromatography approaches like HPTLC and UV Spectrophotometry methods are also used for assay of Venlafaxine.

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