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## **A REVIEW ON PIROXICAM, VENLAFAXINE IN BULK AND FORMULATION BY USING DIFFERENT ANALYTICAL METHODS**

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### **ABSTRACT**

The review article deals with the estimation of NSAIDS like piroxicam and antidepressants like venlafaxine in bulk and varied dosage forms by using different analytical techniques. Piroxicam is a chemically unique, long-acting, strong anti-inflammatory /analgesic drug that is now available for the treatment of arthritis and other inflammatory infections. Determination and estimation of piroxicam, venlafaxine by using different analytical methods like UV-Visible spectrophotometer, High Performance Liquid Chromatography [HPLC], High performance thin layer chromatography [HPTLC], Liquid chromatography -Mass Spectroscopy [LC-MS], Gas chromatography [GC].

**Keywords: Antidepressants, NSAIDS, Piroxicam, Venlafaxine, Chromatography**

### **INTRODUCTION:**

Nonsteroidal anti-inflammatory drugs, or NSAIDs, are the most prescribed pain relievers. NSAIDs are a highly successful medicine class for pain and inflammation, but they are also known to cause gastrointestinal bleeding, cardiovascular side

effects, and NSAID-induced nephrotoxicity. Nonsteroidal anti-inflammatory medications (NSAIDs) are a class of analgesics and anti-inflammatory pharmaceuticals that are widely used to treat pain, inflammation, and other conditions in humans, as well as fever.

These medications have a low acidity substance with pK values between 3-6 because of their carboxylic groups or ketoenol tautomeric structure [3]. These medications inhibit Cyclooxygenases (COXs) enzymes, which are rate-determining enzymes for prostaglandins and other prostanoids synthesis, such as thromboxane's [1].

### PIROXICAM

Piroxicam [4-hydroxy-2-methyl-N-(2-pyridyl)-H-1,2-benzothiazine-3-carboxamide-1,1-di-oxide] is a potent non-steroidal anti-inflammatory and analgesic

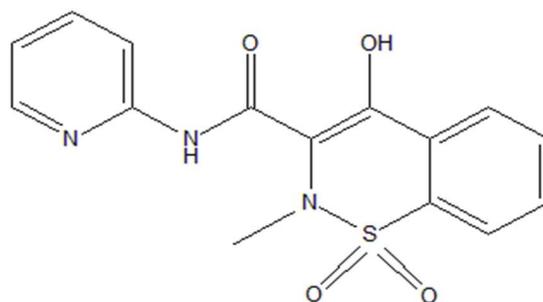


Figure 1: Structure of Piroxicam

### ANTIDEPRESSANTS

Antidepressants are drugs that can help with depression, social anxiety disorder, anxiety disorders, seasonal affective disorder, dysthymia, or mild persistent depression, among other things. They try to address chemical imbalances in the brain's neurotransmitters, which are thought to be the cause of mood and behavior abnormalities [4].

agent of molecular weight (C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>S=331.35 g/mol) [2]. Piroxicam, a non-selective nonsteroidal anti-inflammatory medication (NSAID), binds to and chelates both isoforms of cyclooxygenases (COX1 and COX2), halting phospholipase A2 activity and the conversion of arachidonic acid into prostaglandin precursors at the rate-limiting cyclooxygenase enzyme step. Piroxicam inhibits neutrophil activation, which contributes to its overall anti-inflammatory benefits (Figure 1).

### VENLAFAXINE

Venlafaxine is a bicyclic phenylethylamine derivative which inhibits presynaptic reuptake of noradrenaline (norepinephrine), serotonin (5-hydroxytryptamine; 5-HT). This facilitates neurotransmission by prolonging the engagement of these neurotransmitters with postsynaptic receptor sites. The etiology of depressive illness has been linked to dysregulation of these neurotransmitters [5] (Figure 2).

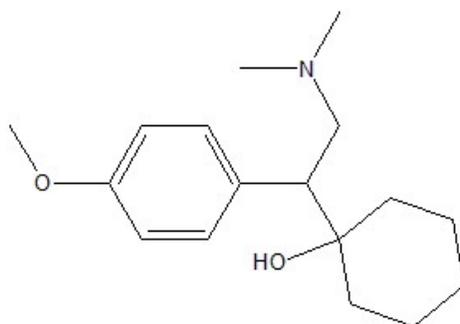


Figure 2: Structure of Venlafaxine

Table 1: Methods for the determination of piroxicam, venlafaxine by UV

S. No.	DRUG	APPLICATION	DESCRIPTION	REF.NO
1.	Piroxicam in cyclodextrin complexes	Inclusion complex	Detection wavelength: 334nm Solvent: acetonitrile Linearity: 2.0 µg/ml, 6.0 µg/ml, 10.0 µg/ml	[6]
2.	Piroxicam	Formulation	Detection wavelength: 200-500nm Solvent: water Linearity: 10-20 mg/L	[7]
3.	piroxicam	Impurity in bulk material, suppositories	Detection wavelength: 240, 244nm Solvent: ethanol Column: $5 \times 10^{-5}$ M	[8]
4.	Piroxicam, zolmitriptan	Formulation	Detection wavelength: 320nm Solvent: water Linearity: Piroxicam: 2, 4, 6, 8, 10 µg/ml Zolmitriptan: 1, 2, 3, 4, 5 µg/ml	[9]

Table 2: Methods for the estimation of piroxicam, venlafaxine by HPLC method

S. No.	DRUGS	DESCRIPTION	REF.NO.
5.	Piroxicam	Detection wavelength: 240nm Column: Phenomenex Luna C18 Mobile phase: A: 10mM potassium dihydrogen orthophosphate pH 3.0 B: acetonitrile Flow rate: 1.0ml/min Linearity: 1-5 µg/ml	[10]
6.	piroxicam	Detection wavelength: 486nm Column: Hypersil Gold, 5-µm 150x4mm column Mobile phase: Trifluoroacetic acid: acetonitrile 60:40 (v/v) Flow rate: 1.1ml/min Linearity: 0.25, 0.5, 1, 2.5, 5, 10, 25 µg/ml	[11]
7.	Piroxicam	Detection wavelength: 360nm Column: SB-C <sub>18</sub> Eclipse (150x4.6; 5µm) reversed phase stainless steel column Mobile phase: acetonitrile: water (50:50v/v) Flow rate: 0.5ml/min Linearity: 5-90 µg/ml	[12]
8.	Piroxicam	Detection wavelength: 363nm Column: 5µm CN (spherisorb) microbore column Mobile phase: acetonitrile: water mixture (6: 94, v/v) Flow rate: 0.5ml/min Linearity: 0.05-10 µg/ml	[13]
9.	Piroxicam	Detection wavelength: 247nm Column: Spherisorb NH <sub>2</sub> (250mmx4.6mm) Mobile phase: Buffer: methanol (40:60 v/v)	[14]

		Flow rate:1.0ml/min Linearity: $1.15 \times 10^{-5}$ M	
10.	Piroxicam	Detection wavelength:230nm Column: C <sub>18</sub> column Mobile phase: Methanol: water (70:30v/v) Flow rate:2.0ml/min Linearity:0.5,1.0,1.5,2.0,2.5,3.0µg/ml	[15]
11.	Piroxicam	Detection wavelength:361nm Column: Reversed phase C <sub>18</sub> column Mobile phase: Methanol-10mm phosphate buffer pH 2 (45:55v/v) Flow rate:1.5ml/min Linearity:0.02-20µg/ml	[16]
12.	Piroxicam	Detection wavelength:254nm Column: Reversed-phase C <sub>18</sub> column Mobile phase: aqueous buffer/methanol (55:45 v/v) Flow rate:1.2ml/min Linearity:1 -150µg/ml	[17]
13.	piroxicam	Detection wavelength:360nm Column: Kromasil C18 column Mobile phase: acetonitrile:20 mM phosphate buffer pH 3.1 (50:50, v/v) Flow rate:1.0ml/min Linearity:0.05,0.1,0.15,0.2,0.5,1.0,1.5,2.5µg/ml	[18]
14.	venlafaxine	Detection wavelength:225nm Column: Kromasil KR 100-5C18 column Mobile phase: Acetonitrile: methanol (90:10v/v) Flow rate:1.0ml/min Linearity:200µg/ml	[19]
15.	venlafaxine	Detection wavelength:228nm Column: Ascentis C18 column (150 mm × 4.6 mm) Mobile phase: 30% acetonitrile in 20mM phosphate buffer pH 6.5 Flow rate:1.0ml/min Linearity:1.05-10.5µg/ml	[20]
16.	venlafaxine	Detection wavelength:235nm Column: Kromasil 100-5C18 column Mobile phase: 60% methanol: acetonitrile (95:5v/v) Flow rate:0.7ml/min Linearity:0.5-25 ng/µl	[21]
17.	Venlafaxine, Duloxetine, Fluoxetine, Paroxetine	Detection wavelength:235nm Column: Inertsil ODS -3 Column Mobile phase: Acetonitrile: ammonium acetate (41:59 v/v) Flow rate:1.3ml/min Linearity:0.1-20 ng/ml	[22]
18.	Venlafaxine	Detection wavelength:228nm Column: Ascentis C18 column (150 mm × 4.6 mm) Mobile phase: 30% acetonitrile in 20 mM potassium phosphate buffer Flow rate:1.0ml/min Linearity:1.05-10.5 µg/ml	[23]
19.	Venlafaxine	Column: CHRIOBIOTIC V Mobile phase: 30 mmol/l ammonium acetate-methanol (15:85, pH 6.0) Flow rate:1.0ml/min Linearity:5.0-400 ng/ml	[24]
20.	Venlafaxine	Detection wavelength:229nm Column: Zorbax XDB C-18 column Mobile phase: 62% water containing 0.05 M potassium dihydrogen phosphate, 28% methanol, and 10% isopropyl alcohol Flow rate:1.0ml/min Linearity:5-1000 ng/ml	[25]
21.	Venlafaxine	Detection wavelength:226nm Column: C-18 column Mobile phase: Acetonitrile: phosphate buffer Flow rate:1.0ml/min	[26]

Linearity:1-1000ng/ml			
22.	Venlafaxine	Detection wavelength:229nm Column: Spherisorb S5 C8 analytical column Mobile phase: acetonitrile–phosphate buffer (30:70, v/v) Flow rate:1.4ml/min	[27]
23.	Venlafaxine	Detection wavelength:229nm Column: Supelcosil LC-8DB column Mobile phase: 20% acetonitrile in 0.1 M ammonium acetate Linearity:10-500ng/ml	[28]
24.	Piroxicam, 5-hydroxy piroxicam	Detection wavelength:353nm Column: CNW C <sub>18</sub> RP (250 mm × 4.6 mm, 5 μm) Mobile phase: Acetonitrile:Trifluoro acetic acid (62:38v/v) Flow rate:1.0ml/min Linearity:1.50-2.50μg/ml	[29]

Table 3: Methods for the estimation of venlafaxine by HPTLC

S. No.	DRUGS	DESCRIPTION	REF.NO
25.	Venlafaxine	Mobile phase: butanol–acetic acid–water 6:2:2 (v/v) Linear range:100–600 ng per band Correlation coefficient (r) ± SD 0.9984 ± 0.0004	[30]

Table 4: Methods for the estimation of venlafaxine by LC-MS/MS

S. No.	DRUGS	DESCRIPTION	REF.NO
26.	Venlafaxine	Column: C18 (150x4.6mm) Mobile phase: 10mM ammonium formate: methanol (20:80 v/v) Flow rate: 0.800 ml/min	[31]

Table 5: Methods for the estimation of venlafaxine by UPLC-MS

S. No.	DRUGS	DESCRIPTION	REF.NO
27.	venlafaxine	Column: BEH Shield RP18 (1.7 mm, 100 mmx 2.1 mm) Mobile phase: water containing 2mM ammonium acetate: acetonitrile (20:80% v/v) Flow rate: 0.3ml/min Ion source: electrospray ionization	[32]

Table 6: methods for the estimation of venlafaxine by Gas chromatography

S. No.	DRUGS	DESCRIPTION	REF.NO.
28.	Venlafaxine, viloxazine, imipramine, desipramine, sertraline, amoxapine	Linearity: 100-2000ng/ml Solvent: methanol Column: Chem Elut CE 1010 columns Flow rate :1.5ml/min	[33]

Table 7: Methods for the estimation of Piroxicam, Venlafaxine by combined UV, HPLC methods

S. No.	DRUGS	DESCRIPTION FOR UV	DESCRIPTION FOR HPLC	REF. NO.
29.	Piroxicam	Wavelength range:480nm Mobile phase:Phosphate buffer: ethanol, 90:10, v/v.	Wavelength range: 254nm Mobile phase: phosphate buffer (pH 7.0, 0.05 M): methanol, 60:40, v/v	[2]
30.	Piroxicam	Wave length :333nm Linearity:10.0-100.0μg/ml	Column: LiChroCART®125-4 Mobile phase: methanol:(buffer solution citric acid-dibasic sodium phosphate pH 3.0) 55:45 ratio	[34]
31.	Venlafaxine	Wave length:225nm Linearity:50 -160μg/ml Regression coefficient :0.999	Column: C <sub>18</sub> Mobile phase: phosphate buffer (pH: 3.6)-acetonitrile (60: 40, v/v) Flow rate:1ml/min	[35]

Table 8: Method for the estimation of venlafaxine by HPLC-MS/MS

S. No.	DRUGS	DESCRIPTION	REF.NO.
32.	Venlafaxine	Column: vancomycin chiral column (5 mm, 250x4.6 mm) Flow rate:1.0ml/min Mobile phase: methanol-water containing 30 mmol/L ammonium acetate (8:92 v/v) Lower limit of quantification:0.28ng/ml	[36]

## CONCLUSION

This review article examined about the techniques obtained for the estimation of piroxicam, venlafaxine in bulk and pharmaceutical dosage forms. Various spectroscopic methods like UV Spectroscopy, Chromatographic techniques like HPLC, HPTLC and hyphenation techniques like LC-MS/MS, HPLC-MS/MS, UPLC-MS, combined UV and HPLC method are established. Among all the techniques HPLC with UV detection was widely used by using methanol, acetonitrile, phosphate buffer as mobile phases. For compounds separation and detection 0.5-2.0 ml/min flow rate is maintained. This article can be more favorable for more analytical investigations.

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## REFERENCES

[1] Supakanya

Wongrakpanich, Amarporn

Wongrakpanich., (2018). "A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drug

Use in The Elderly", US National library of medicine, 9(1), Pp.143-150.

[2] Hasan Basan, Nilgun Gunden Goger.,

(2001). "Quantitative determination of piroxicam in a new formulation (piroxicam-β-cyclodextrin) by derivative UV spectrophotometric method and HPLC", Journal of pharmaceutical and biomedical analysis, 26, Pp.171-178.

[3] ArJn Gül Dal, Zeynep Oktayer.,

(2014). "Validated Method for the Determination of Piroxicam by Capillary Zone Electrophoresis and Its Application to Tablets", Journal of analytical methods in chemistry, Pp.1-7.

[4] Zachary M. Sheffler; Sara Abdijadid.,

(2021). "Antidepressants", National center for biotechnology information.

[5] Stephen M. Holliday and Paul

Benfield., (1995). "Venlafaxine a review of its pharmacology and therapeutic potential in depression", Adis international limited, 49(2), Pp.280-294.

- [6] Thierry Van Hees, Geraldine Piel., (2002). "Determination of the free/included piroxicam ratio in cyclodextrin complexes: comparison between UV spectrophotometry and differential scanning calorimetry", journal of pharmaceutical sciences,15, Pp.347-353.
- [7] Pretty Falena Atmanda Kambira, Dion Notario., (2020). "Combination uv-vis spectroscopy and partial least square for detecting adulteration paracetamol and piroxicam in traditional medicines", journal of pharmaceutical sciences and community, 17(1), Pp.41-50.
- [8] Caducei G, Colanzi A., (1989). "Determination of 2-aminopyridine in piroxicam by derivative UV-spectrophotometry", international journal of pharmaceutics,53, Pp.257-259.
- [9] Bhupinder Bhyan, D.C. Bhatt., (2021). "Method Development and Validation for Simultaneous Estimation of Zolmitriptan and Piroxicam by UV Spectrophotometric Method", gradiva review journal, Pp.160-167.
- [10] Mallesh Kurakula, Abdul Bari Mohd., (2011). "Estimation of piroxicam in proliposomal formulation using RP HPLC Method", international journal of chemical and analytical science,2(9), Pp.1193-1196.
- [11] George Traian Alexandru Burcea Dragomiroiu, Adina Cimpoiesu., (2015). "The development and validation of a rapid HPLC method for determination of piroxicam", farmacia, vol. 63,1.
- [12] Alina Diana Panainte, Madalina Vieriu., (2017). "Fast HPLC method for the determination of piroxicam and its application to stability study",68, no.4.
- [13] Wanwimolruk, S., wanwimolruk, S.Z., Zoest, A.R., (2006). "a simple and sensitive Hplc assay for piroxicam in plasma and its application to bioavailability study", journal of liquid chromatography,14(12), Pp.2373-2381.
- [14] Stavroula Rozou, Afrodite Voulgari., (2003). "The effect of pH dependent molecular conformation and dimerization phenomena of piroxicam on the drug: cyclodextrin complex stoichiometry and its chromatographic behavior". A new

- specific HPLC method for piroxicam: cyclodextrin formulations, *European journal of pharmaceutical sciences*, Pp.661-669.
- [15] Saeed Arayne, M., Najma Sultana., (2005). "Determination and quantification of piroxicam in tablets by RP-HPLC", *Journal of Indian chem.*, vol.82, Pp.838-841.
- [16] Massoud Amanlou A, Ahmad Reza Dehpour U., (1997). "Rapid method for the determination of piroxicam in rat plasma using high-performance liquid chromatography", *journal of chromatography B*, 696, Pp.317-319.
- [17] Jeffrey A. Richards, Dale A. Cole., (1987). "High Performance Liquid Chromatography Assay for Piroxicam in Pharmaceutical Products", *journal of chromatographic sciences*, vol 25, Pp.292-295.
- [18] Yritia. M, Parra. P., (1999). "Piroxicam quantitation in human plasma by high-performance liquid chromatography with on- and off-line solid-phase extraction", *journal of chromatography A*, 846, Pp.199-205.
- [19] Nageswara Rao. R, Narasa Raju. A., (2006). "Simultaneous separation and determination of process-related substances and degradation products of venlafaxine by reversed-phase HPLC", *Journal of Separation Science*, 29, Pp.2733-2744.
- [20] Ebenezer B. Asafu-Adjaye a, Patrick J. Faustino., (2007). "Validation and application of a stability-indicating HPLC method for the in vitro determination of gastric and intestinal stability of venlafaxine", *journal of pharmaceutical and biomedical analysis*, 43, Pp.1854-1859.
- [21] Samanidou, Nazyropoulou & Kovatsi., (2011). "A simple HPLC method for the simultaneous determination of venlafaxine and its major metabolite O-desmethylvenlafaxine in human serum", *bioanalysis*, 3(15), Pp.1713-1718.
- [22] Samaniodu, Kourti., (2009). "Rapid HPLC method for the simultaneous monitoring of duloxetine, venlafaxine, fluoxetine and paroxetine in biofluids", *bioanalysis*, 1 (5), Pp.905-917.

- [23] Ebenezer B. Asafu-Adjaye., (2007). "Validation and application of a stability-indicating HPLC method for the in vitro determination of gastric and intestinal stability of venlafaxine", Journal of Pharmaceutical and Biomedical Analysis, 43, Pp.1854-1852.
- [24] Liu Wen, Wang Feng., (2007). "Simultaneous stereoselective analysis of venlafaxine and O-desmethylvenlafaxine enantiomers in human plasma by HPLC-ESI/MS using a vancomycin chiral column", journal of chromatography B, 850, Pp.183-189.
- [25] Raut B. B, Kolte. B. L., (2003). "A Rapid and Sensitive HPLC Method for the Determination of Venlafaxine and O-Desmethylvenlafaxine in Human Plasma with UV Detection", Journal of liquid chromatography and related technologies, Vol. 26, No. 8, Pp.1297-1313.
- [26] Ewelina Dziurkowska Marek Wesolowski., (2013). "Simultaneous quantitation of venlafaxine and its main metabolite, O-desmethylvenlafaxine, in human saliva by HPLC", Journal of Separation Science, 36, Pp.1726-1733.
- [27] Matoga. M, Pehourcq. F., (2001). "Rapid high-performance liquid chromatographic measurement of venlafaxine and O-desmethylvenlafaxine in human plasma Application to management of acute intoxications", Journal of Chromatography B, 760, Pp.213-218.
- [28] David R. Hicks, Donna Wolaniuk., (1994). "A high-performance liquid chromatographic method for the simultaneous determination of venlafaxine and ortho - Desmethylvenlafaxine in biological fluids", therapeutic drug monitoring, vol 6, Pp.100-107.
- [29] Naila Shahbaz., (2018). "Simultaneous Determination of Piroxicam and 5-hydroxyproxicam: HPLC/UV Method Development, Validation and Application for Pharmacokinetic Evaluation in Pakistani Population", Journal of the chemical society of Pakistan, vol 40, Pp.856-865.
- [30] Bokka Ramesh, Panguluri Sreeman Narayana., (2011). "Stability-Indicating HPTLC Method for

- Analysis of Venlafaxine Hydrochloride, and Use of the Method to Study Degradation Kinetics”, *Journal of planar chromatography*, 2, Pp.160-165.
- [31] Gaurang R. Shah, Bharat T. Thaker., (2009). “Simultaneous determination of venlafaxine and its main active metabolite 0-Desmethyl venlafaxine in rat plasma by LC-MS/MS”, *Analytical sciences*, vol.25, Pp.1207-1210.
- [32] Sunil Kumar Dubeya, R.N. Saha., (2013). “Rapid sensitive validated UPLC–MS method for determination of venlafaxine and its metabolite in rat plasma: Application to pharmacokinetic study”, *Journal of Pharmaceutical Analysis*,3(6), Pp.466-471.
- [33] Martfnez M.A, Siinchez de la Torre. C., (2002). “Simultaneous Determination of Viloxazine, Venlafaxine, Imipramine, Desipramine, Sertraline, and Amoxapine in Whole Blood: Comparison of Two Extraction/Cleanup Procedures for Capillary Gas Chromatography with Nitrogen-Phosphorus Detection”, *Journal of Analytical Toxicology*, Pp.296-302.
- [34] Erika Rosa Maria Hackmann A, Elizabeth A. dos Santos Gianotto., (1993). “Determination of Piroxicam in Pharmaceutical Preparations By ultraviolet direct spectrophotometry, ultraviolet difference spectrophotometry and High performance Liquid Chromatography”, *Analytical letters*,26(2), Pp.259-269.
- [35] Maryam HOSSEIN., (2011). “Application of UV-spectrophotometry and HPLC for determination of venlafaxine and its four related substances in pharmaceutical dosage forms”, *journal of pharmaceutical sciences*,8(2), Pp.91-104.
- [36] Wen Liu, Ying-Chun Dai., (2010). “Development and validation of a HPLC-MS/MS method for the determination of venlafaxine enantiomers and application to a pharmacokinetic study in healthy Chinese volunteers”, *biomedical chromatography*, Pp.412-416.