A REVIEW ON CHROMATOGRAPHIC ESTIMATION OF SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS IN BULK AND IN DIFFERENT DOSAGE FORMS

Shivani C Patel*, Dr. Dilip G. Maheshwari †
Department of Quality Assurance, L. J. Institute of Pharmacy, Ahmedabad, Gujarat, India
Email: dgmaheshwari@gmail.com

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Abstract:
Nowadays antidepressant drugs like selective serotonin reuptake inhibitors (SSRIs) represent the first choice in the treatment of moderate to severe depressive illness, various phobias, and personality disorders. This review includes most of the published analytical methods for estimation of SSRIs based on high-performance liquid chromatography coupled with UV, fluorescence and mass spectrometry detectors, capillary electrophoresis, gas chromatography with mass spectrometry detectors among others and high performance thin layer chromatography. Thus, this paper will help in the selection and development of proper analytical methodologies for estimation of SSRIs to achieve satisfactory results.

Key words: Selective Serotonin Reuptake Inhibitors (SSRIS), High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), high performance thin layer chromatography (HPTLC), ultraviolet spectroscopy (UV), liquid chromatography–mass spectroscopy (LCMS)

Introduction:
Selective serotonin re-uptake inhibitors or serotonin-specific reuptake inhibitors (SSRIs) are a class of compounds typically used as antidepressants in the treatment of major depressive disorder and anxiety disorders. SSRIs ease depression by affecting naturally occurring chemical messengers (neurotransmitters), which are used to communicate between brain cells. SSRIs block the reabsorption (reuptake) of the neurotransmitter serotonin in the brain. Changing the balance of serotonin seems to help brain cells send and receive chemical messages, which in turn boosts mood. Most antidepressants work by changing the levels of one or more of these neurotransmitters. SSRIs are called selective because they seem to primarily affect serotonin, not other neurotransmitters. SSRIs have the power to markedly improve mood, outlook, and behavior in people with depression. SSRIs are believed to increase the
extracellular level of the neurotransmitter serotonin by limiting its reabsorption into the presynaptic cell, increasing the level of serotonin in the synaptic cleft available to bind to the postsynaptic receptor. They have varying degrees of selectivity for the other monoamine transporters, with pure SSRIs having only weak affinity for the norepinephrine and dopamine transporters. Use of SSRIs is, the main indication for SSRIs is major depressive disorder. SSRIs are prescribed for anxiety disorders, such as social anxiety disorder, panic disorders, obsessive–compulsive disorder (OCD), eating disorders, chronic pain and occasionally, for posttraumatic stress disorder (PTSD). Anti-depressants are recommended as an alternative or additional first step to self-help programs in the treatment of bulimia nervosa.

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Drug</th>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Paroxetine Hydrochloride</td>
<td>HPLC</td>
<td><strong>Stationary Phase:</strong> C18 (5 mm, 15 cm6.0 mm) column</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mobile phase:</strong> sodium dihydrogen phosphate:methanol:acetonitrile (5:1:4 v/v/v)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Flow rate:</strong> 1.0 ml/min</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Detection wavelength:</strong> 237 nm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Retention Time:</strong> 6.60 ± 0.04 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Linearity:</strong> 2×10⁻⁷ - 6×10⁻⁵</td>
</tr>
<tr>
<td>2</td>
<td>Citalopram In Tablets</td>
<td>HPLC, Densitometric HPTLC, and Video densitometric HPTLC</td>
<td><strong>FOR HPLC</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Stationary Phase:</strong> Waters Nova-Pak C18 column</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mobile phase:</strong> methanol–0.067 M phosphate buffer pH 2.00 (55:45, v/v)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Detection wavelength:</strong> 239 nm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Linearity Range:</strong> 5–50 µg/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>FOR HPTLC</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Stationary Phase:</strong> silica gel 60F254 HPTLC plates</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mobile phase:</strong> benzene–acetone–ethanol– 25% aqueous ammonia (45:40:10:5, v/v/v/v)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Detection wavelength:</strong> 226 nm (densitometry) and 254 nm (videodensitometry)</td>
</tr>
<tr>
<td>3</td>
<td>Paroxetine In Human Plasma</td>
<td>LC-MS/MS</td>
<td><strong>Stationary Phase:</strong> C18 packed in a (50 x 2.0 mm) Polaris 5 µm particle size column</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mobile phase:</strong> acetonitrile: water (6:4; v/v)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Flow rate:</strong> 0.15 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Run Time:</strong> 2.6 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Retention Time:</strong> 1.6 and 1.7 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>% Recovery:</strong> 87.34%</td>
</tr>
<tr>
<td>4</td>
<td>Sertraline In Human Plasma</td>
<td>HPLC and Electrospray Ionization Mass Spectrometry</td>
<td><strong>Stationary Phase:</strong> C18 column (5 µm, 150- × 4.6-mm i.d.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mobile phase:</strong> methanol–10 mmol/L ammonium acetate solution–acetonitrile (62:28:10, v/v/v).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Concentration Range:</strong> 0.5–25 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Correlation Coefficient:</strong> 0.9998.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Flow rate:</strong> 1 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>LOD:</strong> 0.2 ng/mL</td>
</tr>
<tr>
<td>No.</td>
<td>Drug Description</td>
<td>Method</td>
<td>Parameters</td>
</tr>
<tr>
<td>-----</td>
<td>--------------------------------------</td>
<td>-----------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 5   | Peroxetine In Human Plasma           | HPLC            | **LOQ:** 0.5 ng/mL  
**Retention Time:** 5.7 and 2.5 min  
**Stationary Phase:** C18 column  
**Mobile phase:** acetonitrile:water (70:30)  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 567 nm  
**Concentration Range:** 2000 ng/m  
**Retention Time:** 1.1 and 15.5 minutes |
| 6   | Fluvoxamine In Human Plasma And Urine| RP-HPLC         | **LOD:** 1.4 and 1 ng/ml for plasma and urine  
**LOQ:** 5 and 2 ng/ml for plasma and urine  
**Stationary Phase:** Phenomenex C18 (250 mm × 4.6 mm i.d., 5 µm particle size) column  
**Mobile phase:** acetonitrile/water (80:20 v/v)  
**Flow rate:** 1 ml/min  
**Concentration Range:** 5–145 and 2–100 ng/ml  
**Detection wavelength:** 215 nm  
**Injection Volume:** 10 μl  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  |
| 7   | Sertraline And Its Cis- (1r, 4r) Enantiomer | HPLC            | **LOD:** 30 ng/ml  
**LOQ:** 120 ng/ml  
**% Recovery:** 93.8 to 103.9%  
**Stationary Phase:** Chiralpak AD-H (250 x 4.6 mm, 5 µm particle size) column  
**Mobile phase:** hexane, isopropyl alcohol, ethanol and diethyl amine (850:100:50:0.1 v/v/v/v)  
**Injection Volume:** 10 μl  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  |
| 8   | Citalopram And Its S – Enantiomer Escitalopram | Fluorimetric and Thin Layer Chromatography Densitometric Methods | **FOR HPTLC:**  
**Stationary Phase:** (10 × 10 cm, aluminum plate coated with 0.25 mm silica gel F254)  
**Mobile phase:** acetonitrile-water (17:3 v/v)  
**Flow rate:** 1 ml/min  
**Linearity range:** 0.50–40.00 µg/spot  
**Correlation Coefficient (r):** 0.9997  
**LOD:** 0.014  
**LOQ:** 0.046  
**Detection wavelength:** 254 nm  
**Fluorimetric method:**  
**Detection wavelength:** 242 nm  
**Concentration Range:** 0.125–16.25 µg mL⁻¹ and 0.125–12.50 µg mL⁻¹  
**Linearity range:** 0.125–16.250 µg mL⁻¹  
**Correlation Coefficient (r):** 0.9998  
**LOD:** 0.017  
**LOQ:** 0.056  |
| 9   | Fluoxetine In Capsule Dosage Form     | HPTLC           | **LOD:** 0.017  
**LOQ:** 0.056  
**Detection wavelength:** 254 nm  
**Correlation co-efficient (r):** 0.9986  
**Linearity range:** 4-20 g/spot  
**% Recovery:** 100.0 ± 0.01%  
**Stationary Phase:** Silica gel G60 F254 aluminium foil  
**Mobile phase:** acetonitrile: chloroform in the ratio of 1:9  
**Detection wavelength:** 254 nm  
**Concentration Range:** 0.125–16.25 µg mL⁻¹ and 0.125–12.50 µg mL⁻¹  
**Linearity range:** 4-20 g/spot  
**% Recovery:** 100.0 ± 0.01%  |
| 10  | Sertraline                            | HPLC            | **Stationary Phase:** orbax Bonus-RP column (150 mmx4.6mm, 5 microm)  
**Mobile phase:** phosphate buffer :methanol  
**LOD:** 30 ng/ml  
**LOQ:** 120 ng/ml  
**% Recovery:** 93.8 to 103.9%  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  
**Flow rate:** 1.0 ml/min  
**Detection wavelength:** 215 nm  |

**Note:** The parameters mentioned are specific to the analysis of the drugs and their enantiomers using various chromatographic techniques.
<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Method</th>
<th>Details</th>
</tr>
</thead>
</table>
| 11 | Fluoxetine And Its Active Metabolite Norfluoxetine In Human Urine | GC-MS analysis | Stationary Phase: HP5MS fused silica capillary column (30m x 250 μm i.d. x 0.25 μm film thickness).  
Flow rate: 1.0 mL/min  
Detection wavelength: 220 nm  
Linearity range: 5-75 ng mL-1 for fluoxetine and 6-125 ng mL-1 for norfluoxetine  
LOD: 1-10 ng mL-1  
LOQ: 5-10 ng mL-1  
% Recovery: 87 - 109% |
| 12 | Fluoxetine Hydrochloride In Bulk And Pharmaceutical Formulation | HPTLC | Stationary Phase: silica gel G60F254 TLC precoated plates (20x10)  
Mobile phase: Acetone: Methanol (5:4, v/v)  
Detection wavelength: 226nm  
Linearity range: 0.3-2.1 μg/mL  
Correlation Coefficient (r²): 0.999  
% Recovery: 99.94± 1.188% |
| 13 | Citalopram Hbr | RP-HPLC | Stationary Phase: C18 column  
Mobile phase: methanol: phosphate buffer (pH 3.4) : acetonitrile (55:40:5 v/v/v)  
Flow rate: 1.35ml/min  
Detection wavelength: 254nm  
Retention Time: 3.741min  
Concentration Range: 10-50 μg/ml |
| 14 | Citalopram In Relevance To Pharmaceutical Analysis | UV & GC | FOR GC:  
Stationary Phase: SE-30 column (1 m x 3 mm i.d)  
Carrier Gas: Nitrogen  
Flow rate: 40 ml/min  
Retention Time: 12.8 min  
Linearity: 200-400 μg/ml  
LOD: 1.1726 μg/ml  
LOQ: 3.5535 μg/ml  
% Recovery: 98.36–100.07%  
FOR UV:  
Detection wavelength: 240 nm  
Linearity: 2-4 μg/ml  
LOD: 40.59 ng/ml  
LOQ: 123.0 ng/ml  
% Recovery: 98.53–100.78% |
| 15 | Escitalopram Oxalate In Dosage Forms | HPLC | Wavelength: 238nm  
Mobile phase: Phosphate Buffer  
Stationary phase: Xterra RP 18  
Solvent System:  
Acetonitrile:Methanol(1:1) (v/v)  
Flow rate: 1.2 ml/min.  
Stationary phase: Xterra RP 18 |
| 16 | Escitalopram Oxalate In Tablet Dosage Forms | RP-HPLC | Wavelength: 226nm  
Mobile phase: Methanol: Disodium Hydrogen Phosphate: Acetonitrile (28:44:28v/v/v)  
Stationary phase: Hypersil BDS C8  
Flow rate: 1.5ml/min |
<table>
<thead>
<tr>
<th>17</th>
<th>Sertraline</th>
<th>RP-HPLC &amp; UV</th>
<th><strong>Injection Volume</strong>: 20μL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stationary Phase</strong>:</td>
<td>LiChroCART column (250 × 4.6 mm ID) with Purospher (RP-18e, 5 μm)</td>
<td><strong>Mobile phase</strong>: methanol/water (75:25, v/v)</td>
<td><strong>Detection wavelength</strong>: 273 nm</td>
</tr>
<tr>
<td><strong>Concentration Range</strong>:</td>
<td>10–200 μg ml⁻¹</td>
<td><strong>Detection wavelength</strong>:</td>
<td><strong>Correlation Coefficient</strong>: 0.998</td>
</tr>
<tr>
<td><strong>LOD</strong>:</td>
<td>28 ng/ml</td>
<td><strong>LOQ</strong>: 85.5 ng/ml</td>
<td><strong>Retention Time</strong>: 1.75 and 2.0 min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18</th>
<th>Dapoxetine Hydrochloride</th>
<th>HPTLC DENSITOMETRIC METHOD</th>
<th><strong>Stationary Phase</strong>: aluminium plates pre coated with silica gel 60 F254</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mobile phase</strong>: Chloroform: Methanol: Acetonitrile: Formic acid (4: 0.8: 4: 1 v/v/v/v)</td>
<td><strong>Detection wavelength</strong>: 232 nm</td>
<td><strong>Concentration Range</strong>: (ng/spot) 150 – 750 and 450 – 2250</td>
<td><strong>Correlation Coefficient</strong>: (r²) 0.9995 0.9980</td>
</tr>
<tr>
<td><strong>Linearity range</strong>: 150-750 ng/spot and 450-2250 ng/spot</td>
<td><strong>LOD</strong>: 21.86 and 128.58 ng/spot</td>
<td><strong>LOQ</strong>: 66.25 ng/spot and 389.64 ng/spot</td>
<td><strong>% Recovery</strong>: 99.58 – 100.72 % and 99.97 – 100.21%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>19</th>
<th>Citalopram</th>
<th>RP-HPLC</th>
<th><strong>Stationary Phase</strong>: Agilent Eclipse XDB C18 (150 x 4.6 mm; 5μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mobile phase</strong>: Acetate buffer (pH 4.5): Acetonitrile (65:35 v/v)</td>
<td><strong>Detection wavelength</strong>: 240nm</td>
<td><strong>Concentration Range</strong>: 25 – 150 μg/mL</td>
<td><strong>Flow rate</strong>: 1.0 mL/min</td>
</tr>
<tr>
<td><strong>Column Temperature</strong>: 30°C</td>
<td><strong>Run time</strong>: 8 min</td>
<td><strong>Column Temperature</strong>:</td>
<td><strong>Retention Time</strong>: 3.72 min</td>
</tr>
<tr>
<td><strong>Injection volume</strong>: 10 μL</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>20</th>
<th>Peroxetine</th>
<th>HPLC</th>
<th><strong>Stationary Phase</strong>: chromosil C18 column (250 mm x 4.6 mm, 5μ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mobile phase</strong>: Ortho Phosphoric acid:Acetonitrile:Methanol(35:40:25)</td>
<td><strong>Detection wavelength</strong>: 255nm</td>
<td><strong>Concentration range</strong>: 1-7ppm</td>
<td><strong>Flow rate</strong>: 1 ml/min</td>
</tr>
<tr>
<td><strong>Detection range</strong>:</td>
<td><strong>Run time</strong>: 7 min</td>
<td><strong>Run time</strong>: 2.911 min</td>
<td><strong>Injection Volume</strong>: 20 μl</td>
</tr>
<tr>
<td><strong>Flow rate</strong>:</td>
<td><strong>LOQ</strong>: 0.33ppm</td>
<td><strong>Retention Time</strong>:</td>
<td><strong>LOD</strong>: 0.1ppm</td>
</tr>
<tr>
<td>1.0 ml/min</td>
<td><strong>LOD</strong>: 0.005 ng/mL</td>
<td>--</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>21</th>
<th>Paroxetine</th>
<th>HPLC with Electrochemical Detection</th>
<th><strong>Stationary Phase</strong>: Kromasil C18 column (5m particle size, 120mm × 4.6mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mobile phase</strong>: acetonitrile: water (40:60)</td>
<td><strong>Electrochemical Detection</strong>: at 0.9 V</td>
<td><strong>Flow rate</strong>: 1.0 ml/min</td>
<td><strong>Retention Time</strong>: 7.20 ± 0.10 min</td>
</tr>
<tr>
<td><strong>Flow rate</strong>:</td>
<td><strong>LOD</strong>: 0.005 ng/mL</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>1.0 ml/min</td>
<td>--</td>
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</tr>
<tr>
<td>Page</td>
<td>Method</td>
<td>Stationary Phase</td>
<td>Mobile phase</td>
</tr>
<tr>
<td>------</td>
<td>-----------------</td>
<td>-------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>22</td>
<td>Fluoxetine And Its N-Demethylated Metabolite (Norfluoxetine)</td>
<td>HPTLC</td>
<td>Aluminium backed silica gel 60 F254 TLC plates, (20 cm x 10 cm, layer thickness 0.2 mm)</td>
</tr>
<tr>
<td>23</td>
<td>Citalopram Hydrobromide In Bulk Dosage Forms</td>
<td>RP-HPLC-PDA</td>
<td>Agilent Eclipse XDB C18 column (150 x 4.6mm, 5µm)</td>
</tr>
<tr>
<td>24</td>
<td>Fluoxetine Hydrochloride in Oral Solution</td>
<td>RP-HPLC</td>
<td>Zorbax eclipse plus-C8 (250x4.6) mm; 5µm column</td>
</tr>
<tr>
<td>25</td>
<td>Sertraline</td>
<td>RP-HPLC</td>
<td>C18Develosil ODS HG-5 RP 150mm x 4.6mm 5µm particle size</td>
</tr>
<tr>
<td>26</td>
<td>Dapoxetine Hcl In Pharmaceutical Product</td>
<td>STABILITY INDICATING HPLC-UV METHOD</td>
<td>C-18 column</td>
</tr>
<tr>
<td>Page</td>
<td>Drug Name</td>
<td>Formulation</td>
<td>Method</td>
</tr>
<tr>
<td>------</td>
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</tr>
<tr>
<td>27</td>
<td>Dapoxetine</td>
<td>Pure And Solid Dosage Form</td>
<td>HPTLC</td>
</tr>
<tr>
<td>28</td>
<td>Citalopram</td>
<td>Bulk and its Pharmaceutical Dosage Form</td>
<td>RP-HPLC</td>
</tr>
<tr>
<td>29</td>
<td>Fluvoxamine</td>
<td>Pharmaceutical Dosage Forms</td>
<td>RP-HPLC</td>
</tr>
<tr>
<td>30</td>
<td>Fluvoxamine Maleate</td>
<td>In Tablet</td>
<td>FORCE DEGRADATION STUDY AND RP-HPLC</td>
</tr>
<tr>
<td>31</td>
<td>Paroxetine</td>
<td>In Human Serum</td>
<td>HPTLC</td>
</tr>
<tr>
<td>32</td>
<td>Paroxetine</td>
<td>And Its 4-Hydroxy-3-Methoxy Metabolite</td>
<td>HPLC</td>
</tr>
</tbody>
</table>
SRIs have been used in the treatment of stroke patients, including those with and without symptoms of depression. SSRIs are effective for the treatment of premature ejaculation. SSRIs includes Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline. This paper gives an overview of various analytical methods for estimation of SSRIs. Different methods have been developed for determination of SSRIs like UV-Spectroscopy, liquid Chromatography, HPTLC and LC-MS.

Reported methods are categorized depending on the following considerations:

1. SSRIs analyzed by UV-Spectroscopy methods and Chromatographic method.
2. Analysis of SSRIs from combination formulation by UV-Spectroscopy methods and Chromatographic method.
Table-1: Analysis of single component SSRIs by chromatographic method.

Analysis of SSRIs in combined dosage form by chromatographic methods

TABLE 2: Analysis of SSRIs in combined dosage form by chromatographic methods

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Drug Description</th>
<th>Method</th>
<th>Description</th>
<th>Ref. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fluoxetine, Fluvoxamine, And Clomipramine In Pharmaceutical Formulations</td>
<td>GC</td>
<td>Carrier gas: helium, 43.6 cm/s, 80 kPa, 1.2 mL/min, gas flow. Flow rate: 50 mL/min. Concentration range: 0.5–80 mg/L. Linearity range: 0.5–80 mg/L. LOD: 9.75 mg/L and 101.0 mg/L and 38.5 mg/L. LOQ: 26.5 mg/L and 248.0 mg/L and 66.0 mg/L respectively. % Recovery: 97.5–102.5%</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>Fluoxetine and Norfluoxetine in Human Liver Microsomes</td>
<td>Ion-Interaction RP-HPLC</td>
<td>Stationary Phase: ODS silica-based column is Mobile phase: 5.00 mM octylamine in water/acetonitrile (60/40 v/v), at pH = 6.4, Flow rate: 1 ml/min Detection wavelength: 230 nm LOD: 5 µg/ml % Recovery: 94-104%</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>Fluvoxamine And Fluvoxamino Acid In Human Plasma</td>
<td>RP-HPLC</td>
<td>Stationary Phase: C18 bonded-solid phase cartridge Flow rate: 1 ml/min Detection wavelength: 254 nm Concentration Range: 25.0-200.0 ng/mL</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>Fluvoxamine And Paroxetine In Human Serum</td>
<td>HPLC &amp; UV</td>
<td>Stationary Phase: Ultracep ES 100 CN column Mobile phase: acetonitrile/methanol/phosphate buffer (58/19/23, v/v/v) Flow rate: 1.5 ml/min Detection wavelength: 220 nm LOD: 5 and 2 µg/L % Recovery: m± 8%</td>
<td>39</td>
</tr>
<tr>
<td>5</td>
<td>Fluoxetine Hydrochloride and Olanzapine In Tablet Dosage Forms</td>
<td>RP-HPLC and HPTLC</td>
<td>FOR RP-HPLC Mobile phase: acetonitrile:methanol:0.032 M ammonium acetate buffer (45:05:50, v/v/v) Flow rate: 1.5 ml/min Detection wavelength: 235 nm Concentration Range: 0.2-4 and 0.1-2 µg/ml for Fluoxetine HCL and Olanzapine FOR HPTLC Stationary Phase: Merck TLC aluminium sheets of silica gel 60 F254 Mobile phase: acetone: methanol: triethyleamine (5:3:0.5, v/v/v) Detection wavelength: 235 nm Concentration Range: 300-1000 and 150-500 ng/spot respectively.</td>
<td>40</td>
</tr>
</tbody>
</table>
|   | Fluoxetine Hydrochloride and Olanzapine in Tablet Dosage Forms. | RP-HPLC and HPTLC | FOR RP-HPLC:
Mobile phase: Acetonitrile:Methanol:0.032 M ammonium acetate buffer (45:05:50, v/v/v)
Flow rate: 1.5 ml/min
Detection wavelength: 235 nm
Concentration Range: 0.2-4 μg/ml
*Fluoxetine Hydrochloride* and 0.1-2 μg/ml *Olanzapine* respectively.

FOR HPTLC:
Stationary Phase: Merck TLC aluminium sheets of silica gel 60 F254
Mobile phase: acetone: methanol: triethyleamine (5:3:0.5, v/v/v)
Concentration Range: 300-1000 ng/spot for *fluoxetine* and 150-500 ng/spot for *Olanzapine* respectively.

| 7 | Fluoxetine Hydrochloride and Olanzapine In Combined Dosageforms | Stability-Indicating HPLC | Stationary Phase: C18 column
Mobile phase: 75 mM potassium dihydrogen phosphate buffer (pH 4.0):acetonitrile:methanol (55:40:5, v/v/v)
Flow rate: 0.8 mL/min
Detection wavelength: 227 nm

| 8 | Alprazolam And Sertraline In Pure Powder And Tablet Formulations | HPLC and HPTLC | FOR HPLC:
Stationary Phase: Nucleosil C18 column (150 mm long, 4.6 mm i.d., and 5-μm particle size)
Mobile phase: acetonitrile and phosphate buffer(5:5)
Flow rate: 1.0 mL/min
concentration range: 3–18 μg/mL
%Recovery: 101.86 ± 0.21 and 100.57 ± 0.31% for ALZ and SER, respectively

FOR HPTLC:
Stationary Phase: silica gel 60 F254
Mobile phase: acetone/toluene/ammonia (6.0:3.0:1.0, v/v/v)
Detection wavelength: 230 nm
concentration range: 400–1400 ng/spot
%Recovery: 101.32 ± 0.15 and 100.38 ±0.51% for ALZ and SER, respectively

| 9 | Citalopram Hydromide And Dothiepin Hydrochloride In Human Plasma | HPLC | Stationary Phase: Phenomenex C-18 column (250 x 4.6 mm)
Mobile phase: acetonitrile: water (35:65 v/v)
Detection wavelength: 234 nm
Flow rate: 1 ml/min
LOD: 7.978 and 26.595 ng/ml respectively
LOQ: 11.413 and 38.044 ng/ml respectively.

| 10 | Fluoxetine And Norfluoxetine In Plasma | RP-HPLC Employing Pre-Column Derivatization for UV- | Stationary Phase: HIQ sil ODS column (250 mm length x 4.6 mm internal diameter)
Mobile phase: acetonitrile: water: triethylamine: 0.01 M Orthophospheric acid

<p>| | | | |
|   |   |   |   |</p>
<table>
<thead>
<tr>
<th><strong>Sensitivity Enhancement</strong></th>
<th><strong>(O.P.A.)</strong> (70:30:0.5:2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flow rate:</strong> 1 ml/min</td>
<td><strong>Detection wavelength:</strong> 227 nm</td>
</tr>
<tr>
<td><strong>Retention Time:</strong> 2.49 and 4.24 min respectively.</td>
<td></td>
</tr>
</tbody>
</table>

**Tadalafil And Dapoxetine In Tablet Dosage Form**

**RP-HPLC**

- **Stationary Phase:** Phenomenax Luna C18 (150mmx 4.6 mm i.d, particle size 5 mcm) column
- **Mobile phase:** acetonitrile: buffer (Ammonium acetate PH 7.0) in the ratio of 70:30(v/v)
- **Flow rate:** 1.0ml/min
- **Detection wavelength:** 241 nm
- **Concentration range:** 4-16mcg/ml and 12-48mcg/ml
- **Injection volume:** 20 µl
- **Retention Time:** 3.713min and 11.453min
- **LOD:** 1.194 mcg/ml and 3.6815 mcg/ml
- **LOQ:** 0.93608mcg/ml and 2.8366 mcg/ml
- **% Recovery:** 99.54 and 99.17 % respectively.

**Escitalopram And Clonazepam In Pharmaceutical Formulation**

**RP-HPLC**

- **Wavelength:** 248 nm
- **Stationary phase:** C18 column
- **Flow rate:** 1ml/min
- **Solvent System:** Methanol :Buffer (pH 4.0) 90:10 (v/v).
- **Concentration range:** 2.5-80 µg mL⁻¹ and 0.125-4 µg mL⁻¹ respectively.
- **Run Time:** 10 min.

**Escitalopram And Etizolam In Bulk And Tablet Dosage Form**

**RP-HPLC**

- **Wavelength:** 254 nm.
- **Stationary phase:** C18 column
- **Flow rate:** 1.0 ml/min
- **Mobile phase:** Acetonitrile: Hexane Sulfonic Acid 0.005 M pH 3.0 (40:60 v/v)
- **Concentration Range** :20-160µg/ml for ESC and 2-16 µg/ml for ETI
- **Injection volume** : 10 µl
- **Run time** :10.0 min
- **LOD:** ESC and ETI were found to be 0.23 µg/ml and 0.04 µg/ml respectively.
- **LOQ:** 0.68 µg/ml and 0.11 µg/ml respectively.
- **Retention Time:**3.66 and 8.07 min
- **% Recovery:** 100.86% for ESC and 98.78-100.24% for ETI

**Fluoxetine Hydrochloride And Olanzapine In Capsules**

**RP-HPLC and HPTLC**

- **FOR HPLC**
  - **Stationary Phase:** C18 column
  - **Mobile phase:** phosphate buffer pH 4.0 :acetonitrile :triethylamine (53:47:0.03v/v/v)
  - **Flow rate:** 1.0 ml/min
  - **Detection wavelength:** 235 nm
- **FOR HPTLC**
  - **Stationary Phase:** C18 column
<table>
<thead>
<tr>
<th>Step</th>
<th>Compound Details</th>
<th>Method</th>
<th>Stationary Phase</th>
<th>Mobile Phase</th>
<th>Detection Wavelength</th>
<th>Retention Time</th>
<th>Linearity Range</th>
<th>Correlation Coefficient</th>
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<td>Dapoxetine Hydrochloride And Tadalafil Hydrochloride In Tablet Dosage Form</td>
<td>RP-HPLC</td>
<td>octa decyl silane [C18 250x 4mm i.d. 5µ column</td>
<td>methanol: toluene: ammonia (7:3:0.1v/v/v)</td>
<td>235 nm</td>
<td></td>
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<td>16</td>
<td>Vardenafil Hydrochloride And Dapoxetine Hydrochloride In Combined Pharmaceutical Dosage Form</td>
<td>Spectrophotometry And RP-HPLC</td>
<td>RP-18 e (5µm)</td>
<td>Methanol: Acetonitrile 95:5 with 0.5% TEA</td>
<td>280 nm</td>
<td>4.46 and 10.11 min</td>
<td>8-48 μg/mL and 24-144 μg/mL respectively</td>
<td>0.997 and 0.998 respectively</td>
<td>0.225 μg/ml and 0.163 μg/ml</td>
<td>0.682 μg/ml and 0.494 μg/ml</td>
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<tr>
<td>17</td>
<td>Avanafil And Dapoxetine Hydrochloride In Bulk And Dosage Form</td>
<td>RP-HPLC</td>
<td>C18, (250 mm x 4.6 mm i.d. and 5µm particle size)</td>
<td>acetonitrile:water (90:10, v/v)</td>
<td>238 nm</td>
<td>2.90 and 4.17 min</td>
<td>2-12µg/ml and 1.2-7.2µg/ml respectively</td>
<td>0.999</td>
<td>0.069 and 0.13 μg/ml</td>
<td>0.21 and 0.42 μg/ml</td>
<td>101.82% 100.77%</td>
</tr>
<tr>
<td>18</td>
<td>Escitalopram And Etizolam In Bulk And Table Dosage Form</td>
<td>RP-HPLC</td>
<td>C18 column</td>
<td>Potassium dihydrogen orthophosphate: Acetonitrile (40:60)</td>
<td>254 nm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>120 µg/ml of Escitalopram oxalate and 6 µg/ml of Etizolam</td>
<td>20 µL.</td>
</tr>
<tr>
<td>Page</td>
<td>Method</td>
<td>Stationary Phase</td>
<td>Mobile phase</td>
<td>Flow rate</td>
<td>Detection wavelength</td>
<td>Linearity Range</td>
<td>Retention Time</td>
<td>LOD</td>
<td>LOQ</td>
<td>% Recovery</td>
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<td>19</td>
<td>Fluoxetine And Olanzapine In Tablet Dosage Form</td>
<td>RP-HPLC</td>
<td>HYPERSIL ODS C18 (250 x 4.6 mm, 5μm)</td>
<td>Phosphate buffer PH 5.8: Acetonitrile (55:45 v/v)</td>
<td>1 ml/min</td>
<td>261 nm</td>
<td>18-42μg/ml and 72-168μg/ml</td>
<td>3.480 and 2.597 min</td>
<td>0.70 and 1.99</td>
<td>2.11 and 6.03</td>
<td>100.3 and 99.3%</td>
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<tr>
<td>20</td>
<td>Fluoxetine And Sildenafil Citrate In Bulk &amp; Tablet Dosage Form</td>
<td>RP-HPLC</td>
<td>Hiber R C-18 columns (150mm x 4.6 mm x 5μm) analytical column.</td>
<td>Acetonitrile: Potassium Dihydrogen Phosphate buffer (50:50 v/v)</td>
<td>1 ml/min</td>
<td>223 nm</td>
<td>3.68 min and 5.31 min respectively.</td>
<td>0.70 and 1.99</td>
<td>2.11 and 6.03</td>
<td>100.3 and 99.3%</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Fluoxetine Hydrochloride And Alprazolam In Pharmaceutical Dosage Form</td>
<td>RP-HPLC</td>
<td>C18 column, Phenomenex (250mm x 4.60mm)</td>
<td>Acetonitrile: Water (75:25 V/V)</td>
<td>1.1 ml/min</td>
<td>224 nm</td>
<td>2.02 and 3.14 min respectively.</td>
<td>0.70 and 1.99</td>
<td>2.11 and 6.03</td>
<td>100.3 and 99.3%</td>
<td></td>
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<td>22</td>
<td>Fluoxetine Hydrochloride And Olanzapine In A Pharmaceutical Formulation</td>
<td>RP-HPLC</td>
<td>C18 column (Inertsil C18 Column, 5μ, 250 mm x 4.6 mm)</td>
<td>Ortho Phosphoric acid:Acetonitrile:Methanol (60:30:10)</td>
<td>1.0 ml/min</td>
<td>225nm</td>
<td>2.19 min and 3.71 min respectively.</td>
<td>0.70 and 1.99</td>
<td>2.11 and 6.03</td>
<td>100.3 and 99.3%</td>
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<td>23</td>
<td>Paroxetine And Clonazepam In Bulk And Its Pharmaceutical Formulations</td>
<td>Stability Indicating Liquid Chromatography</td>
<td>Agilent zorbax sb-c18 (250mmx4.6mmx5 μm) column</td>
<td>Orthophosphoric acid and Methanol (60:40 v/v)</td>
<td>0.8 ml/min</td>
<td>270 nm</td>
<td>3.478min and 3.964 min respectively.</td>
<td>0.70 and 1.99</td>
<td>2.11 and 6.03</td>
<td>100.3 and 99.3%</td>
<td></td>
</tr>
</tbody>
</table>

**24 Sertraline Hydrochloride**

RP-HPLC

Stationary Phase: C18 (4.6 x 250mm, 5 μm)

% Recovery: 99.8% of Escitalopram oxalate and 99.46% of Etizolam

**54**

**55**

**56**

**57**

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**59**
| 25 | Sertraline And Doxofylline In Pharmaceutical Dosage Form | RP-HPLC | Mobile phase: KH2PO4 buffer (pH 3.6) : ACN (40% : 60%)  
Flow rate: 1.0 (ml/min)  
Run time: 5 (min)  
Detection wavelength: 225 nm  
Linearity: 100 -500 µg /mL and 1 – 5 µg /mL respectively.  
LOD: 0.12 µg /mL and 0.42 µg /mL  
LOQ: 0.015 µg /mL and 0.05 µg /mL  
% Recovery: 99.84 % and 100.51 %  
Retention Time: 2.344 min and 3.286 min respectively. |
| 26 | Sertraline And Alprazolam In Its Bulk And Pharmaceutical Dosage Form | RP-HPLC | Stationary Phase: Kromasil C18 Column  
Mobile phase: Phosphate buffer and Acetonitrile in the ratio of (30:70)  
Flow rate: 1 ml/min  
Detection wavelength: 234 nm  
Concentration Range: 100-600 ppm and 12.5-75 ppm respectively.  
Injection Volume: 10 µl  
Run Time: was 7 min  
Retention Time: 2.82 min and 3.93 min  
LOD: 0.58 µg/ml and 0.27 µg/ml  
LOQ: 1.77 µg/ml and 0.82 µg/ml  
% Recovery: 99-100% |
| 27 | Paroxetine Hydrochloride And Clonazepam In Pharmaceutical Dosage Forms | STABILITY-INDICATING HPLC | Stationary Phase: cosmolsil packed column 5c-18 ms II (250x4.6 i.d.)  
Mobile phase: acetonitrile: methanol: phosphate buffer orthophosphoric acid (20:50:30, v/v)  
Flow rate: 1.0 ml/min  
Detection wavelength: 239 nm  
Retention Time: 4.915 and 8.056 min  
Concentration range: 10-60 µg/ml and 10-60 µg/ml  
Linearity range: 10-60 ppm and 10-60 ppm respectively.  
LOD: 0.1379 µg/ml and 0.0677 µg/ml  
LOQ: 0.4180 µg/ml and 0.2051 µg/ml  
% Recovery: 99-100% |
| 28 | Paroxetine And Clonazepam | RP-HPLC | Stationary Phase: Agilent Eclipse XDB (C8) (4.6mm x 150mm, 5m) column  
Mobile phase: buffer (pH7, adjusted with pH) |
<table>
<thead>
<tr>
<th>Compound</th>
<th>Method</th>
<th>Stationary Phase</th>
<th>Mobile phase</th>
<th>Flow rate</th>
<th>Detection wavelength</th>
<th>Retention Time</th>
<th>Linearity Range</th>
<th>% Recovery</th>
<th>LOD</th>
<th>LOQ</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tadalafil And Dapoxetine Hydrochloride In Combined Pharmaceutical Dosage Forms</td>
<td>RP-HPLC</td>
<td>Hypersil BDS C8, 250 x 4.6mm column</td>
<td>Acetonitrile in the ratio of 82:18 v/v</td>
<td>0.8 ml/min</td>
<td>265 nm</td>
<td>5 mins</td>
<td>100-300 µg/mL and 26 µg/mL</td>
<td>100% and 100% respectively</td>
<td>2.752 µg/mL and 2.40 µg/mL</td>
<td>9.174 µg/mL and 8.0 µg/mL</td>
<td>100% and 100% respectively</td>
</tr>
<tr>
<td>Vardenafil And Dapoxetine Hcl In Bulk And In Combined Dosage Form</td>
<td>Stability Indicating RP-HPLC</td>
<td>Hypercil BDS C18, 250 mm x 4.6 mm x 5 µm</td>
<td>Acetonitrile: Triethylamine (55:45:0.1 v/v/v)</td>
<td>1.0 ml/min</td>
<td>254 nm</td>
<td>4.473 min and 5.836 min</td>
<td>50-150 µg/mL and 50-150 µg/mL</td>
<td>99.88% to 100.37% and 99.87% to 100.08% respectively</td>
<td>0.56 and 0.32 µg/mL</td>
<td>0.1 µg/mL and 0.2 µg/mL</td>
<td>99.3% and 99.7% respectively</td>
</tr>
<tr>
<td>Paroxetine Hydrochloride &amp; Clonazepam</td>
<td>RP-HPLC</td>
<td>BDS (250 x 4.6mm, 5µm) column</td>
<td>Buffer and Acetonitrile 35:65(v/v/v)</td>
<td>1.1 ml/min</td>
<td>212 nm</td>
<td>2.597 min and 3.472 min</td>
<td>125-750 µg/ml and 2.5-15 µg/ml</td>
<td>99.3% and 99.7% respectively</td>
<td>0.5 µg/ml and 0.1 µg/ml</td>
<td>0.1 µg/ml and 0.2 µg/ml</td>
<td>99.3% and 99.7% respectively</td>
</tr>
<tr>
<td>Doxofylline And Sertraline In Stability indicating RP-HPLC</td>
<td></td>
<td>Hypersil C18(150 X 4.6 mm i.d., 5µm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>99.3% and 99.7% respectively</td>
<td></td>
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</tbody>
</table>
| 33 | Alprazolam And Fluoxetine Hcl In A Pharmaceutical Formulation | HPLC | **Mobile phase**: sodium dihydrogen orthophosphate buffer: acetonitrile (adjusted to pH 6.0 using orthophosphoric acid) 75:25 v/v.  
**Flow rate**: 1.3 ml/min  
**Detection wavelength**: 234 nm  
**Retention Time**: 2.27 min and 3.36 min respectively.  
**Concentration Range**: 100 - 600 μg/ml and 12.5 - 75.0 μg/ml respectively.  
**LOD**: 0.24 μg/ml and 0.13 μg/ml  
**LOQ**: 0.72 μg/ml and 0.39 μg/ml |
|---|---|---|---|
| 34 | Citalopram And Its Metabolites Desmethylcitalopram And Didesmethylcitalopram In Human Plasma | RP-HPLC | **Stationary Phase**: C8 column (5μ, 150 mm x 4.6 mm)  
**Mobile phase**: Phosphate buffer: Acetonitrile (30:70 pH:4.0)  
**Flow rate**: 1.0 ml/min  
**Detection wavelength**: 229 nm  
**Retention Time**: 2.15 min and 3.14 min respectively  
**Linearity range**: 0.6-1.4 μg/ml and 48 to 112 μg/ml respectively  
**% Recovery**: 99.47 to 101.03% and 98.40 to 100.63% |
| 35 | Escitalopram And Clonazepam In Combined Tablet Dosage Form | UV AND RP-HPLC | **FOR UV**  
**Wavelength**: 238.6 and 308 nm  
**Concentration range**: 10.050.0 and 0.53.0 g/mL for ESC and CLO  
**Solvent system**: methanol and water  
**FOR RP-HPLC**  
**Mobile phase**: acetonitrile 0.005 M tetrabutylammonium hydrogen sulfate (55 + 45, v/v)  
**Stationary phase**: SiL C18 column  
**Concentration range**: 10.060.0 and 0.53.0 g/mL for ESC and CLO  
**Internal Standard**: satranidazole |
Conclusion:
This review represents the reported chromatographic methods; developed and validated for determination of selective serotonin reuptake inhibitors (SSRIs). All the reported method was simple, precise and accurate those mostly emphasize separation techniques like liquid and gas chromatography. The analysis is done on individual and several combinations of SSRIs with other drugs. According to this review mobile phase like, Phosphate buffer, Acetonitrile, methanol and water give better HPLC separation and flow rate 1.0 ml/min is more consistent for getting precise retention time.

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References:
9. Önal, Armağan, Determination of Paroxetine in Human Plasma by High-Performance Liquid Chromatography Using 7,7,8,8-Tetracyanoquinodimethane as the Derivatization Reagent”, Lippincott Williams & Wilkins, Inc, April 2006 - Volume 28 - Issue 2 - pp 180-184
10. evgi atar lu, method or the determination o fluvoxamine in human plasma and urine or application to pharmacoinetetic studies, Journal of pharmaceutical and biomedical analis, march 2007, volume Issue 12

11. Rao BM, Sivaiah Sangaraju, B.M. Shyam Kumar , A Validated Normal Phase Chiral Lc Method For The Enantiomeric Separation of Sertraline And Its Cis- (1r, 4r) Enantiomer on Amylose Based Stationary Phase”, Rasayan j chem , 2009 Vol.2, No.1 , 42-48


14. Facultad de Farmacia, Universidad San Pablo-CEU, Urbanizacin Monteprncepe, Development and validation of a HPLC method for the determination of sertraline and three non-chiral related impurities, Journal of pharmaceutical and biomedical analysis, 10/2010 53(2)122-9


20. Syama Sundar, Development And Validation of Liquid Chromatographic Method For Estimation of Escitalopram Oxalate In Tablet Dosage Forms, International Journal of Pharma and Bio Sciences, Jan -Fab 2011, vol 2,Issue 1


26. Dr Manish S. Bhatia, Smita T. Kumbhar, Development And Validation of A Hptlc Method For The Estimation of Fluoxetine And Its N-Demethylated Metabolite (Norfluoxetine), Department of Pharmaceutical Chemistry, September 2013, 30


35. Sigrid Mennickent, Cristina Cifuentes, Mario Vega, Quantitative Determination of Paroxetine in Human Serum by High-Performance Thin-Layer Chromatography, Journal of Planar Chromatography, 2015,28

36. Mireia Segura, Jordi Ortuño, Magí Farré, Quantitative determination of paroxetine and its 4-hydroxy-3-methoxy metabolite in plasma by high performance liquid chromatography/electrospray ion trap mass spectrometry: application to pharmacokinetic studies, Institut Municipal d'Investigació Mèdica

37. Anders Ljungqvist, Kalyn Sowell, Christopher J.L. Buggé, Determination of Citalopram and its Metabolites Desmethylcitalopram and Didesmethylcitalopram in Human Plasma by Liquid-liquid Extraction and LC/MS/MS.


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56. Raval Kashyap, U.Srinivasa, Kalindi Badodaria, Development And Validation of RP-HPLC Method For Simultaneous Estimation Of Avanafil And Dapoxetine Hydrochloride In Bulk And Dosage Form, world journal of pharmacy and pharmaceutical science, June 2014,28


63. Sameena Kouser, Humera Reshma, Method development and validation of simultaneous determination of Sertraline Hydrochloride and Alprazolam in pharmaceutical dosage form by RP-HPLC, Pelagia Research Library, 2014


68. A. Chenthilnathan, M. Rajeshwari, K. Rama, Validated RP-HPLC Method For Simultaneous Estimation of Tadalafil And Dapoxetine Hydrochloride In Combined Pharmaceutical Dosage Forms, international journal of pharmacy and biological science, APR-JUN, 2014, Issue 2, 72-82


71. Dr. A. Suneetha, Stability indicating rp-hplc method for simultaneous estimation of doxofylline and sertraline in bulk & pharmaceutical dosage forms, International Conference & Exhibition On Biotechnology, August 03-04,2015


73. Anders Ljungqvist, Kalyn Sowell, Christopher J.L. Buggé, Determination of Citalopram and its Metabolites Desmethylcitalopram and Didesmethylcitalopram in Human Plasma by Liquid-liquid Extraction and LC/MS/MS.


Corresponding Author:
Dr. Dilip G. Maheshwari*,

Email: dgmaheshwari@gmail.com