1. SYNONYMS

**CFR:**
Phentermine

**CAS #:**
Base: 122-09-8
Hydrochloride: 1197-21-3

**Other Names:**
Duromine
Ionamin
Linyl
Lipopill
Mirapront
Adipex-p
Fastin

2. CHEMICAL AND PHYSICAL DATA

2.1. CHEMICAL DATA

<table>
<thead>
<tr>
<th>Form</th>
<th>Chemical Formula</th>
<th>Molecular Weight</th>
<th>Melting Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base</td>
<td>C_{10}H_{15}N</td>
<td>149.2</td>
<td>Liquid at room temperature</td>
</tr>
<tr>
<td>Hydrochloride</td>
<td>C_{10}H_{15}N-HCl</td>
<td>185.7</td>
<td>198</td>
</tr>
</tbody>
</table>

2.2. SOLUBILITY

<table>
<thead>
<tr>
<th>Form</th>
<th>A</th>
<th>C</th>
<th>E</th>
<th>H</th>
<th>M</th>
<th>W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base</td>
<td>***</td>
<td>S</td>
<td>S</td>
<td>***</td>
<td>S</td>
<td>SS</td>
</tr>
<tr>
<td>Hydrochloride</td>
<td>***</td>
<td>VS</td>
<td>VSS</td>
<td>***</td>
<td>VS</td>
<td>VS</td>
</tr>
</tbody>
</table>

A = acetone, C = chloroform, E = ether, H = hexane, M = methanol and W = water, VS = very soluble, FS = freely soluble, S = soluble, PS = sparingly soluble, SS = slightly soluble, VSS = very slightly soluble and I = insoluble
3. SCREENING TECHNIQUES

3.1. COLOR TESTS

<table>
<thead>
<tr>
<th>REAGENT</th>
<th>COLOR PRODUCED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marquis</td>
<td>Orange</td>
</tr>
</tbody>
</table>

3.2. CRYSTAL TESTS

<table>
<thead>
<tr>
<th>REAGENT</th>
<th>CRYSTALS FORMED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bismuth iodide in $\text{H}_2\text{SO}_4$</td>
<td>Red rods, with drying rods and dendritic clusters</td>
</tr>
<tr>
<td>Gold chloride in $\text{H}_3\text{PO}_4$</td>
<td>Long serrated blades often spearheaded and some plates</td>
</tr>
<tr>
<td>Platinic chloride in $\text{H}_3\text{PO}_4$</td>
<td>Yellow plates, square cut or elongated hexagons, low birefringence</td>
</tr>
</tbody>
</table>

3.3. THIN LAYER CHROMATOGRAPHY

Visualization

Acidified iodoplatinate spray

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>Relative R$_f$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>System TLC 5</td>
</tr>
<tr>
<td>amphetamine</td>
<td>0.9</td>
</tr>
<tr>
<td>ephedrine</td>
<td>0.6</td>
</tr>
<tr>
<td>methamphetamine</td>
<td>0.6</td>
</tr>
<tr>
<td>phentermine</td>
<td>1.0</td>
</tr>
<tr>
<td>phenylpropanolamine</td>
<td>0.9</td>
</tr>
<tr>
<td>pseudoephedrine</td>
<td>0.7</td>
</tr>
</tbody>
</table>
3.4. GAS CHROMATOGRAPHY

Method PHEN-GCS1

Instrument: Gas Chromatograph operated in split mode with FID

Column: 5% phenyl/95% methyl silicone 10 m x 0.32 mm x 1.5 µm film thickness

Carrier Gas: Hydrogen at 35 cm/sec

Temperature: Injector: 280°C
Detector: 280°C
Oven Program:
1) 120°C initial temperature for 2.0 min
2) Ramp to 280°C at 25°C/min
3) Hold final temperature for 1.5 min

Injection Parameters: Split Ratio = 100:1, 1 µL injected

Samples are to be dissolved in 4:1 chloroform: methanol and filtered.

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>dimethylsulfone</td>
<td>0.26</td>
</tr>
<tr>
<td>amphetamine</td>
<td>0.58</td>
</tr>
<tr>
<td>phentermine</td>
<td>1.00  (1.58 min)</td>
</tr>
<tr>
<td>methamphetamine</td>
<td>1.10</td>
</tr>
<tr>
<td>ephedrine</td>
<td>2.06</td>
</tr>
<tr>
<td>cocaine</td>
<td>4.52</td>
</tr>
<tr>
<td>heroin</td>
<td>5.42</td>
</tr>
</tbody>
</table>

3.5. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method PHEN-LCS1

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 4.6 mm x 150 mm at 35°C
Detector: UV, 207 nm
Flow: 1.0 mL/min
Injection Volume: 3 µL
Buffer: 4000 mL water, 22.5 mL phosphoric acid adjusted to pH 2.3 with triethanolamine
Mobile Phase: Buffer: acetonitrile 84:16

Samples are to be dissolved in methanol then filtered with a 0.45-micron filter.

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>RRT</th>
<th>COMPOUND</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>dimethylsulfone</td>
<td>0.48</td>
<td>methamphetamine</td>
<td>0.87</td>
</tr>
<tr>
<td>pseudoephedrine</td>
<td>0.56</td>
<td>phentermine</td>
<td>1.00 (5.45 min)</td>
</tr>
<tr>
<td>amphetamine</td>
<td>0.73</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. SEPARATION TECHNIQUES

Phentermine is most commonly seen in tablet form with only tablet binders present and can be separated by doing solvent washes. Several adulterants can be isolated from phentermine by the use of solvent washes. For example, caffeine is soluble 1 in 7 of chloroform, while phentermine is very soluble in chloroform.

5. QUANTITATIVE PROCEDURES

5.1. GAS CHROMATOGRAPHY

Method PHEN-GCQ1

Internal Standard Stock Solution:
0.20 mg/mL dimethylphthalate in methanol.

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of phentermine hydrochloride at approximately 0.5 mg/mL using the internal standard stock solution.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution.
If necessary, dilute the sample so the final concentration approximates the standard concentration or falls within the linear range.

Instrument: Gas Chromatograph operated in split mode with FID
**Column:**
5% phenyl/95% methyl silicone 10m x 0.32mm x 0.52µm film thickness

**Carrier gas:**
Helium at 1.0 mL/min

**Temperatures:**
Injector: 280°C
Detector: 280°C
Oven Program:
1) 100°C initial temperature for 0.8 min
2) Ramp to 200°C at 25°C/min
3) Hold final temperature for 1.8 min

**Injection Parameters:**
Split Ratio = 20:1, 1 µL injected

**Typical Retention Time:**
Phentermine: 0.8 min
Dimethylphthalate: 1.90 min

**Linear Range:**
0.1 to 1.5 mg/mL

**Repeatability:**
RSD less than 1.2%

**Correlation Coefficient:**
0.9996

**Accuracy:**
Error less than 5%

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>phentermine</td>
<td>1.00 (0.80 min)</td>
</tr>
<tr>
<td>dimethylphthalate</td>
<td>2.37</td>
</tr>
</tbody>
</table>

5.2. CAPILLARY ELECTROPHORESIS

**Method PHEN-CEQ1**

*Internal Standard Stock Solution:*
0.2 mg/mL thiamine hydrochloride in 0.01 N HCl.

*Standard Solution Preparation:*
Accurately weigh and prepare a standard solution of phentermine at approximately 0.2 mg/mL using the internal standard stock solution.

*Sample Preparation:*
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution.
If necessary dilute the sample so the final concentration approximates the standard concentration or falls within the linear range. Filter sample with 0.45-micron filter.

**Mode:** Free Zone

**Column:** 65 cm x 50 µm fused silica capillary

**Run Buffer:** 100 mM lithium phosphate buffer, pH 2.3 (Prepared by titrating 100 mM phosphoric acid with LiOH to pH 2.3)

**Detector:** UV, 207 nm

**Voltage:** 30 kV

**Temperature:** 15°C air cooled

**Injection:** 5 s hydrodynamic at 50 mbar/sec

**Run Time:** 10 min

**Rinse Time:** 2.5 min

**Linear Range:** 0.366 - 1.85 mg/mL

**Repeatability:** RSD of area less than 2.1%

**Correlation Coefficient:** 0.9998

**Accuracy:** Error less than 5%

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>thiamine</td>
<td>0.78</td>
</tr>
<tr>
<td>phentermine</td>
<td>1.00 (6.65 min)</td>
</tr>
</tbody>
</table>

6. **QUALITATIVE DATA**

See spectra on the following pages for FT-IR, Mass Spectrometry, Nuclear Magnetic Resonance, and Vapor Phase IR.
7. REFERENCES

Fulton, Charles C., Modern Microcrystal Test for Drugs, Wiley-Interscience.


8. ADDITIONAL RESOURCES

Forendex

Wikipedia
Vapor Phase IR
Phentermine
2 mg/mL in CH₃OH

***No Data Available***