# High-throughput approaches towards the definitive identification of pharmaceutical drug metabolites. 3. A rapid methodology for the characterisation of tertiary amine-*N*-oxides containing metabolites using structurally dependent dissociation pathways and reconstructed ion chromatograms

## Supporting information

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## Abstract

Herein, the molecular structures constituting the compound library analysed by QIT-MS/MS and QqTOF-MS are shown. In addition, the relative abundances of the product ions formed through the losses of interest are displayed.

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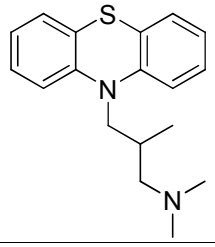
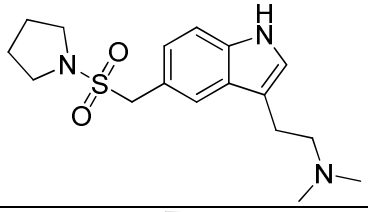
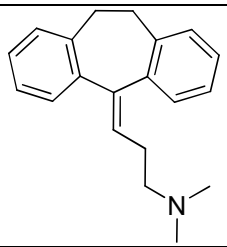
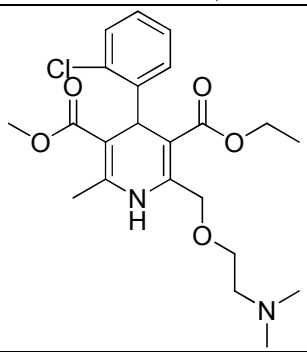
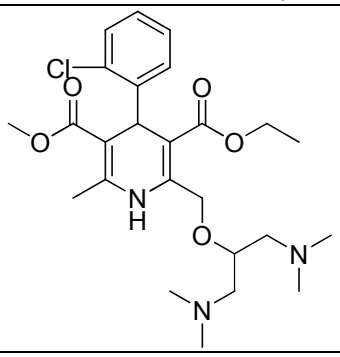
**Table S-1 Molecular structures of compounds containing a dimethylamine substructure**

| Compound | Molecular structure |
|---|---|
| Alimemazine |  |
| Almotriptan |  |
| Amitriptyline |  |
| Amlodipine structural analogue 1 |  |
| Amlodipine structural analogue 2 |  |

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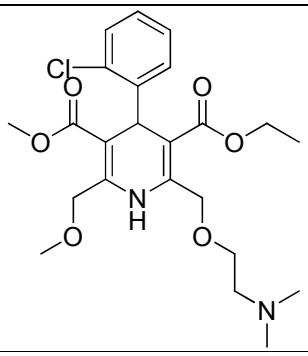
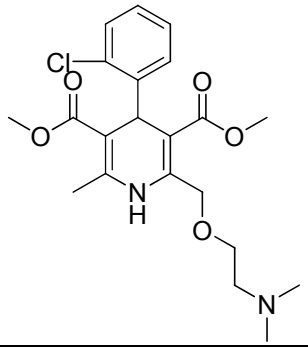
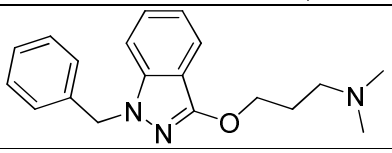
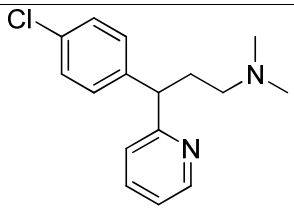
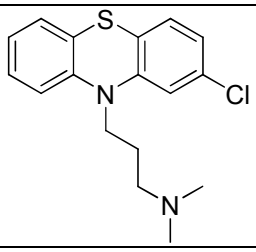
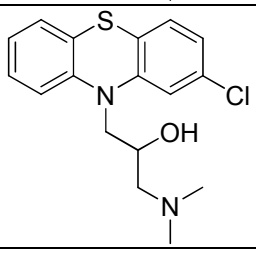
| Amlodipine structural analogue 3 |  |
| Amlodipine structural analogue 4 |  |
| Benzydamine |  |
| Chlorphenamine |  |
| Chlorpromazine |  |
| Chlorpromazine structural analogue 1 |  |

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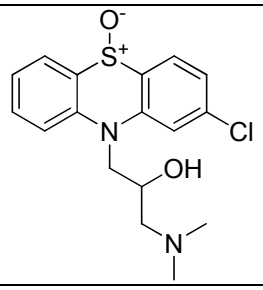
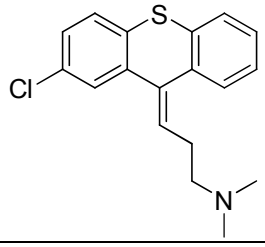
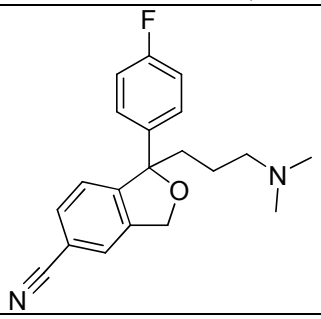
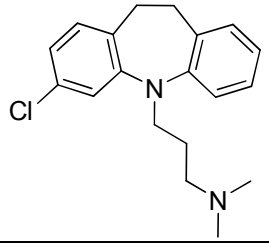
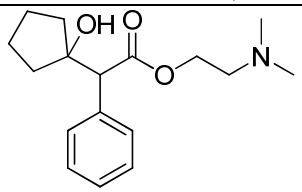
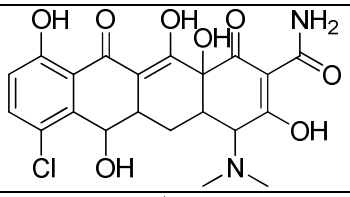
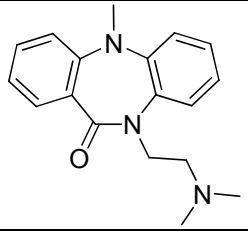
| Chlorpromazine structural analogue 2 |  |
| Chlorprothixene |  |
| Citalopram |  |
| Clomipramine |  |
| Cyclopentolate |  |
| Demeclocycline |  |
| Dibenzepin |  |

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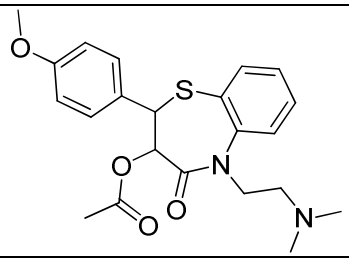
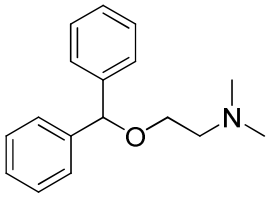
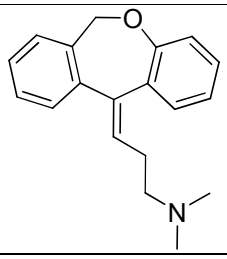
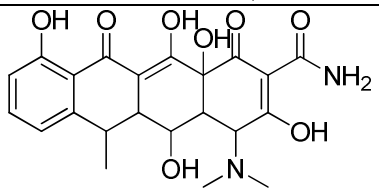
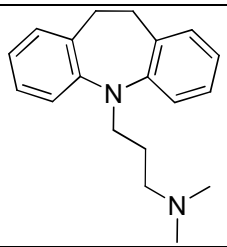
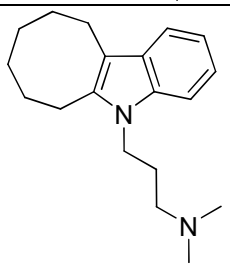
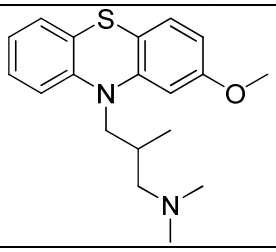
| Diltiazem |  |
| Diphenhydramine |  |
| Doxepin |  |
| Doxycycline |  |
| Imipramine |  |
| Iprindole |  |
| Levomepromazine |  |

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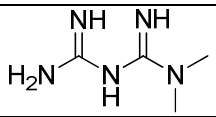
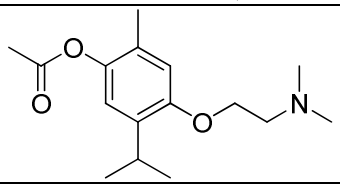
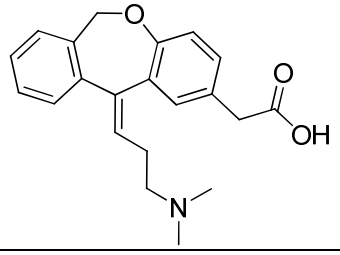
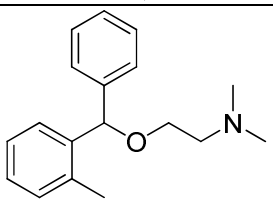
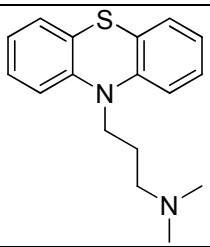
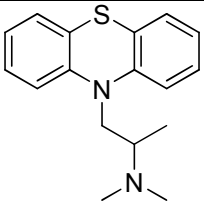
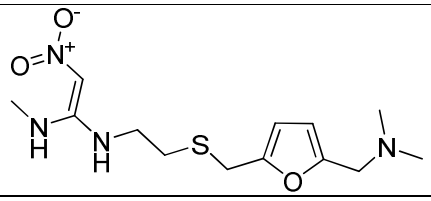
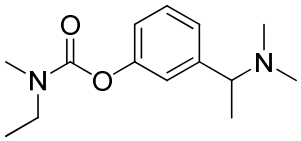
| Metformin |  |
| Moxisylyte |  |
| Olopatadine |  |
| Orphenadrine |  |
| Promazine |  |
| Promethazine |  |
| Ranitidine |  |
| Rivastigmine |  |

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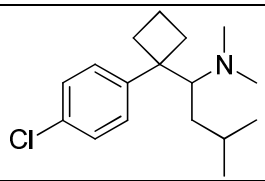
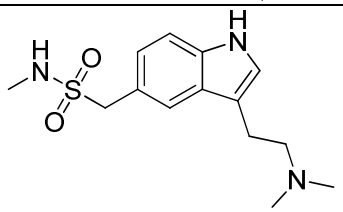
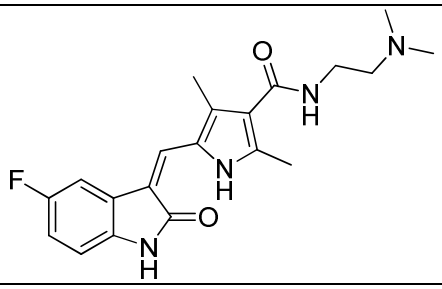
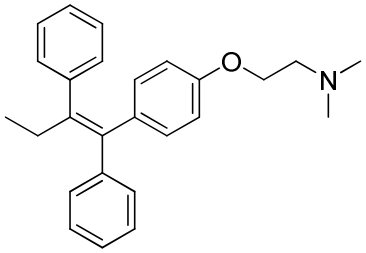
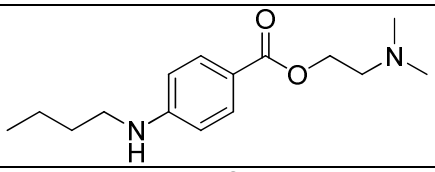
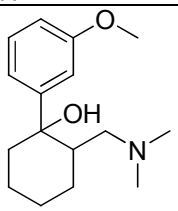
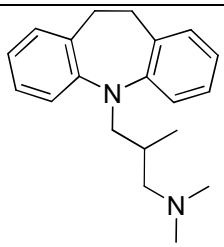
|---|---|
| Sibutramine |  |
| Sumatriptan |  |
| Sunitinib structural analogue |  |
| Tamoxifen |  |
| Tetracaine |  |
| Tramadol |  |
| Trimipramin |  |

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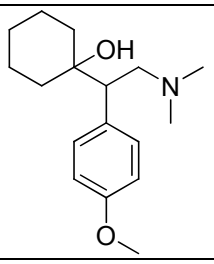
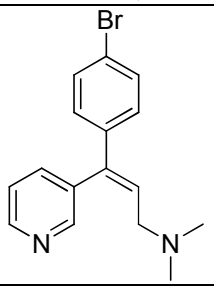
| Venlafaxine |  |
| Zimelidine |  |

**Table S-2 Molecular structures of compounds containing a diethylamine substructure**

| Compound | Molecular structure |
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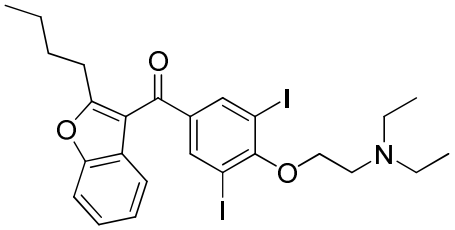
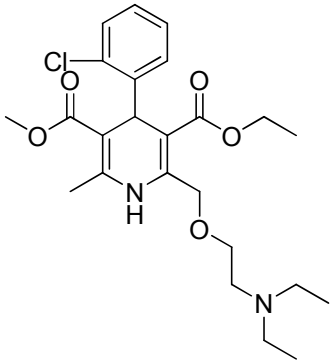
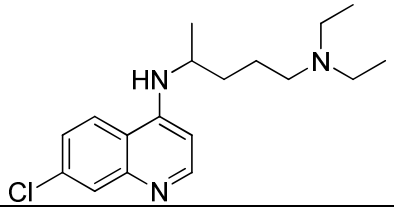
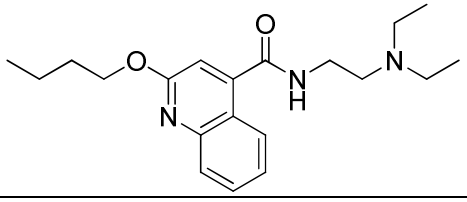
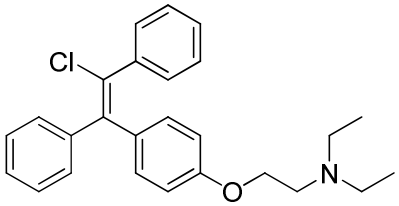
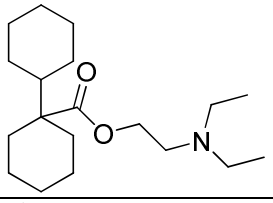
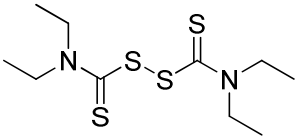
| Amiodarone |  |
| Amlodipine structural analogue 5 |  |
| Chloroquine |  |
| Cinchocaine |  |
| Clomifene |  |
| Dicycloverine |  |
| Disulfiram |  |

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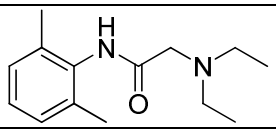
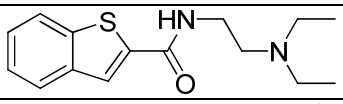
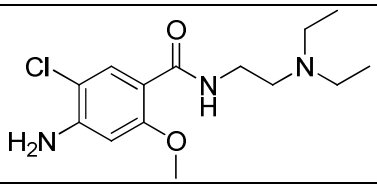
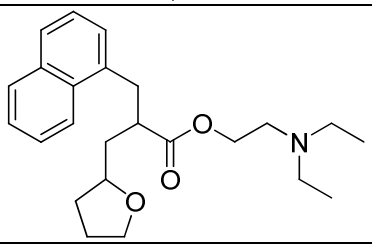
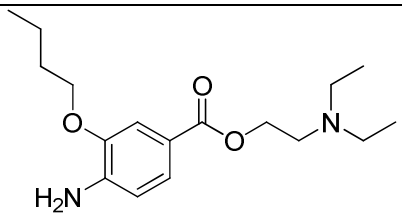
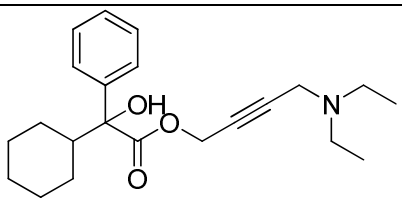
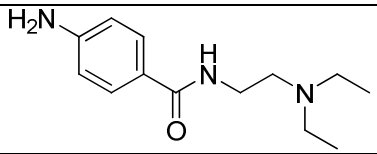
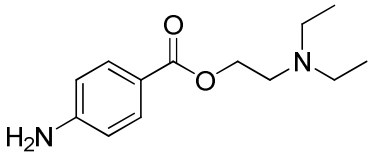
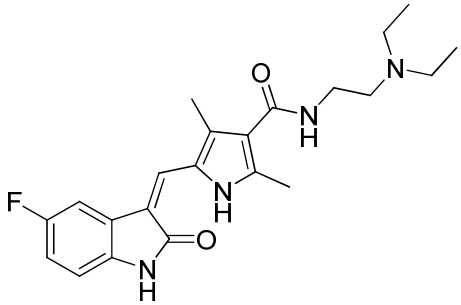
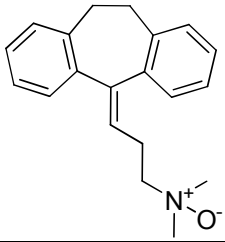
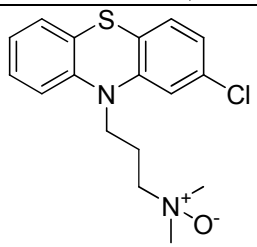
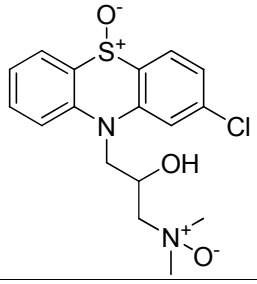
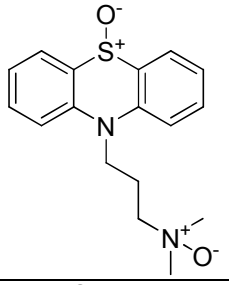
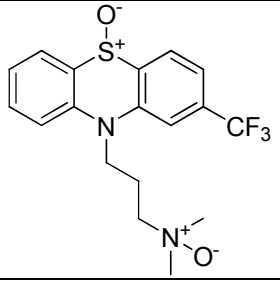
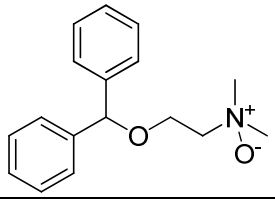
|---|---|
| Lidocaine |  |
| Macrogol |  |
| Metoclopramide |  |
| Naftidrofuryl |  |
| Oxybuprocaine |  |
| Oxybutynin |  |
| Procainamide |  |
| Procaine |  |
| Sunitinib |  |

**Table S-3 Molecular structures of compounds containing an *N*,*N*-dimethylhydroxylamine substructure**

| Compound | Molecular structure |
|---|---|
| Amitriptyline-*N*-oxide |  |
| Chlorpromazine-*N*-oxide 1 |  |
| Chlorpromazine-*N*-oxide 2 |  |
| Chlorpromazine structural analogue-*N*-oxide 1 |  |
| Chlorpromazine structural analogue-*N*-oxide 2 |  |
| Diphenhydramine-*N*-oxide |  |

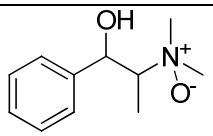
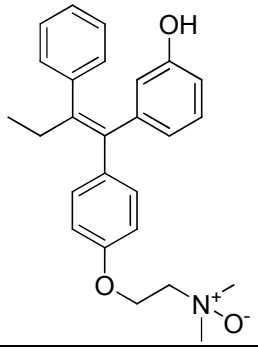
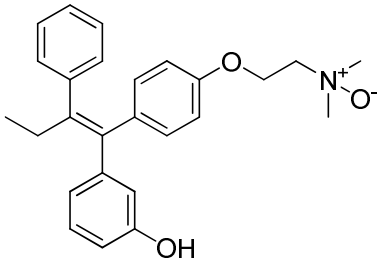
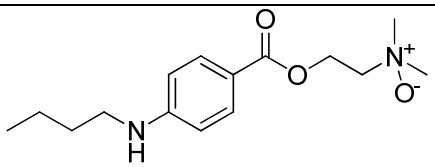
| | |
|---|---|
| Ephedrine structural analogue-*N*-oxide |  |
| Tamoxifen structural analogue-*N*-oxide 1 |  |
| Tamoxifen structural analogue-*N*-oxide 2 |  |
| Tetracaine-*N*-oxide |  |

**Table S-4 Molecular structures of compounds containing an *N*,*N*-diethylhydroxylamine substructure**

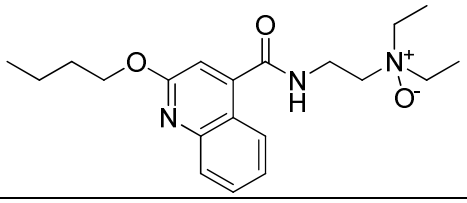
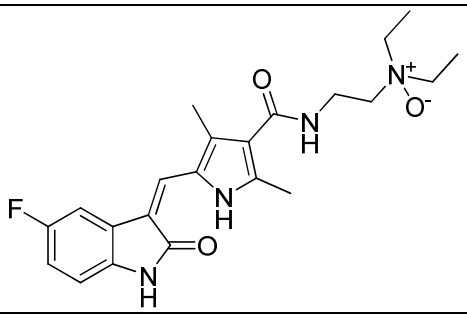
| Compound | Molecular structure |
|---|---|
| Cinchocaine-*N*-oxide |  |
| Sunitinib-*N*-oxide |  |

**Table S-5** **Relative abundances for the product ion formed through the loss of dimethylamine from a series of pharmaceutical compounds using QqTOF-MS and QIT-MS at various collision energies**

| Compound | Relative abundance using QqTOF-MS at 15 eV / % | Relative abundance using QqTOF-MS at 20 eV / % | Relative abundance using QqTOF-MS at 25 eV / % | Relative abundance using QIT-MS at 50%, WideBand activation on / % | Relative abundance using QIT-MS at 50%, WideBand activation off / % |
|---|---|---|---|---|---|
| Alimemazine | 6 | 4 | 1 | 41 | 37 |
| Almotriptan | 52 | 100 | 31 | 17 | 16 |
| Amitriptyline | 76 | 64 | 20 | 100 | 100 |
| Amlodipine structural analogue 1 | 11 | 4 | 1 | 94 | 89 |
| Amlodipine structural analogue 2 | 23 | 18 | - | 100 | 100 |
| Amlodipine structural analogue 3 | 2 | 1 | - | 63 | 71 |
| Amlodipine structural analogue 4 | 5 | 4 | 2 | 100 | 100 |
| Benzydamine | 11 | 5 | 1 | 100 | 100 |
| Chlorphenamine | 100 | 100 | 100 | 100 | 100 |
| Chlorpromazine | 4 | 3 | 2 | 100 | 100 |
| Chlorpromazine structural analogue 1 | - | - | - | 7 | 7 |
| Chlorpromazine structural analogue 2 | 1 | 8 | 3 | 21 | 21 |
| Chlorprothixene | 100 | 100 | 66 | 100 | 42 |
| Citalopram | 8 | 2 | - | 12 | 16 |
| Clomipramine | 6 | 4 | 3 | 100 | 100 |
| Cyclopentolate | - | - | - | - | - |
| Demeclocycline | - | - | - | - | - |

| | | | | | |
|---|---|---|---|---|---|
| Dibenzepin | 100 | 100 | 100 | 100 | 100 |
| Diltiazem | 19 | 3 | - | 18 | 33 |
| Diphenhydramine | - | - | - | - | - |
| Doxepin | 39 | 18 | 9 | 100 | 100 |
| Doxycycline | - | - | 2 | 3 | - |
| Imipramine | 4 | 3 | 2 | 21 | 15 |
| Iprindole | 2 | 4 | 5 | 1 | 1 |
| Levomepromazine | 8 | 4 | 4 | 100 | 99 |
| Metformin | 33 | 23 | 14 | 15 | 14 |
| Moxisylyte | 9 | 5 | 1 | 100 | 100 |
| Olopatadine | 8 | 13 | 6 | 16 | 19 |
| Orphenadrine | - | - | - | - | - |
| Promazine | 7 | 4 | 3 | 55 | 47 |
| Promethazine | 15 | 12 | 5 | 100 | 100 |
| Ranitidine | 7 | 2 | - | 71 | 100 |
| Rivastigmine | 100 | 49 | 11 | 100 | 100 |
| Sibutramine | - | - | - | - | - |
| Sumatriptan | 100 | 71 | 12 | 100 | 81 |
| Sunitinib structural analogue | 100 | 63 | 33 | 89 | 100 |
| Tamoxifen | 2 | 1 | - | 100 | 100 |
| Tetracaine | 11 | 10 | 5 | 16 | 17 |
| Tramadol | - | 2 | - | 16 | - |
| Trimipramin | 4 | 4 | 2 | 21 | 18 |
| Venlafaxine | - | - | - | - | - |
| Zimelidine | 14 | 6 | 3 | 79 | 80 |

**Table S-6** **Relative abundances for the product ion formed through the loss of diethylamine from a series of pharmaceutical compounds using QqTOF-MS and QIT-MS at various collision energies**

| Compound | Relative abundance using QqTOF-MS at 15 eV / % | Relative abundance using QqTOF-MS at 20 eV / % | Relative abundance using QqTOF-MS at 25 eV / % | Relative abundance using QIT-MS at 50%, WideBand activation on / % | Relative abundance using QIT-MS at 50%, WideBand activation off / % |
|---|---|---|---|---|---|
| Amiodarone | - | - | 2 | 100 | 100 |
| Amlodipine structural analogue 5 | 3 | 1 | - | 59 | 61 |
| Chloroquine | 100 | 100 | 100 | 100 | 100 |
| Cinchocaine | 100 | 100 | 81 | 100 | 100 |
| Clomifene | - | 1 | - | 7 | 7 |
| Dicycloverine | 41 | 59 | 24 | 100 | 100 |
| Disulfiram | - | - | - | 18 | 13 |
| Lidocaine | - | - | - | - | - |
| Macrogol | 100 | 100 | 64 | 100 | 100 |
| Metoclopramide | 100 | 100 | 100 | 100 | 100 |
| Naftidrofuryl | 8 | 3 | - | 38 | 55 |
| Oxybuprocaine | 28 | 28 | 26 | 46 | 53 |
| Oxybutynin | - | - | - | - | - |
| Procainamide | 100 | 100 | 51 | 100 | 100 |
| Procaine | 50 | 46 | 21 | 100 | 100 |
| Sunitinib | 100 | 100 | 80 | 100 | 100 |

**Table S-7** **Relative abundances for the product ion formed through the loss of *N*,*N*-dimethylhydroxylamine from a series of pharmaceutical compounds using QqTOF-MS and QIT-MS at various collision energies**

| Compound | Relative abundance using QqTOF-MS at 15 eV / % | Relative abundance using QqTOF-MS at 20 eV / % | Relative abundance using QqTOF-MS at 25 eV / % | Relative abundance using QIT-MS at 50%, WideBand activation on / % | Relative abundance using QIT-MS at 50%, WideBand activation off / % |
|---|---|---|---|---|---|
| Amitriptyline-*N*-oxide | 100 | 65 | 22 | 100 | 100 |
| Chlorpromazine-*N*-oxide 1 | 2 | 5 | 3 | 6 | 5 |
| Chlorpromazine-*N*-oxide 2 | 13 | 52 | 13 | 100 | 100 |
| Chlorpromazine structural analogue-*N*-oxide 1 | 79 | 100 | 26 | 100 | 100 |
| Chlorpromazine structural analogue-*N*-oxide 2 | 32 | 100 | 73 | 100 | 100 |
| Diphenhydramine-*N*-oxide | - | - | - | - | - |
| Ephedrine structural analogue-*N*-oxide | 97 | 30 | 9 | 21 | 19 |
| Tamoxifen structural analogue-*N*-oxide 1 | - | 2 | 1 | 31 | 43 |
| Tamoxifen structural analogue-*N*-oxide 2 | 1 | 2 | 1 | 29 | 35 |
| Tetracaine-*N*-oxide | 100 | 100 | 44 | 100 | 100 |

**Table S-8** **Relative abundances for the product ion formed through the loss of *N*,*N*-diethylhydroxylamine from a series of pharmaceutical compounds using QqTOF-MS and QIT-MS at various collision energies**

| Compound | Relative abundance using QqTOF-MS at 15 eV / % | Relative abundance using QqTOF-MS at 20 eV / % | Relative abundance using QqTOF-MS at 25 eV / % | Relative abundance using QIT-MS at 50%, WideBand activation on / % | Relative abundance using QIT-MS at 50%, WideBand activation off / % |
|---|---|---|---|---|---|
| Cinchocaine-*N*-oxide | 100 | 100 | 96 | 100 | 100 |
| Sunitinib-*N*-oxide | 100 | 100 | 100 | 100 | 100 |