Aim
The aim of this study was to evaluate the concentrations of MDMA found in ante-mortem plasma and post-mortem blood in fatalities admitted to hospital following "Ecstasy" ingestion.

Introduction
3,4-Methylenedioxymethamphetamine (MDMA) is a common component of "Ecstasy" tablets (Figure 1), ingested by the user to achieve a subjective euphoric state with additional empathic effects. "Ecstasy" use has been reported in social settings such as parties and nightclubs for over 15 years. MDMA can exhibit various symptoms including: visual hallucinations, confusion, agitation, sweating, coma and hypothermia. Other common toxic symptoms include hyponatraemia (usual due to excessive water intake) and/or hyperventilation; leading to secondary features such as cerebral oedema, seizures, organ damage and ultimately death. It is also thought that MDMA can precipitate cardiotoxicity in individuals with an existing heart condition. Partly due to variation in MDMA content in tablets, the quantity ingested and any resultant idiosyncratic toxic effects, concentrations of MDMA vary in both non-fatal and fatal cases. Typical concentrations following "recreational" use are less than 0.4 mg/L. In overdose situations, concentrations greater than 2 mg/L may be achieved. Early observations in post-mortem specimens have suggested that MDMA is not necessarily prone to redistribution after death. Such data is mainly based on comparison of concentrations between anatomical sites and have not involved comparison of ante-mortem and post-mortem concentrations. This paper presents both ante-mortem and post-mortem concentrations including data from serial collection times and varying anatomical sites, respectively.

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MDMA and (where possible) MDA concentrations were measured in 5 instances of fatal poisoning following hospital admission (Tables below).

Overall Results
- Reduction with time of MDMA and MDA plasma concentrations during survival period.
- Post-mortem (PM) blood MDMA and MDA concentrations higher than ante-mortem (AM) concentrations in all 5 cases (PM:AM ratio typically between 1 to 2).
- Significant difference between anatomical sites (heart greater than femoral) in Case 3 for both MDMA and MDA.

Note: Difference between PM and AM concentrations may be influenced in part by possible blood-plasma matrix differences.

Conclusions
- There is an apparent rise in MDMA and MDA concentrations after death, regardless of post-mortem collection site. However, the subsequent increase in concentration may vary depending on the anatomical site, indicating possible redistribution.
- Data indicate PM blood concentrations may not accurately relate to concentration either at the time of, or prior to death. Therefore, calculations based on this assumption (e.g. dosage) should not be made.

References

Table: Case Results

<table>
<thead>
<tr>
<th>Sample (site)</th>
<th>MDMA conc. (mg/L)</th>
<th>MDA conc. (mg/L)</th>
<th>Conc. ratio (MDMA)</th>
<th>Conc. ratio (MDA)</th>
<th>Collection time in relation to death (+/- days or hours and mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM Serum</td>
<td>0.52</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>+ 20 minutes</td>
</tr>
<tr>
<td>PM Blood</td>
<td>2.37</td>
<td>NA</td>
<td>PM:AM 1.5</td>
<td>NA</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (left arm)</td>
<td>0.52</td>
<td>NA</td>
<td>PM:AM 1.7</td>
<td>NA</td>
<td>+ 3 days</td>
</tr>
<tr>
<td>AM Serum</td>
<td>0.53</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>+ 10 minutes</td>
</tr>
<tr>
<td>PM Blood</td>
<td>2.01</td>
<td>0.01</td>
<td>PM:AM 1</td>
<td>0.02</td>
<td>+ 10 hours</td>
</tr>
<tr>
<td>PM Blood (femoral)</td>
<td>2.25</td>
<td>0.09</td>
<td>PM:AM 2.5</td>
<td>0.02</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (trunk)</td>
<td>2.99</td>
<td>0.14</td>
<td>PM:AM 2.1</td>
<td>0.14</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (brachial)</td>
<td>2.25</td>
<td>0.19</td>
<td>PM:AM 2</td>
<td>0.17</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (head)</td>
<td>2.19</td>
<td>0.19</td>
<td>PM:AM 2</td>
<td>0.17</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (right)</td>
<td>6.19</td>
<td>0.19</td>
<td>PM:AM 3.2</td>
<td>0.17</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (left)</td>
<td>7.25</td>
<td>0.21</td>
<td>PM:AM 3.5</td>
<td>0.21</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (left)</td>
<td>7.25</td>
<td>0.21</td>
<td>PM:AM 3.5</td>
<td>0.21</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (right)</td>
<td>6.19</td>
<td>0.19</td>
<td>PM:AM 3.2</td>
<td>0.17</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Blood (head)</td>
<td>22.53</td>
<td>1.33</td>
<td>PM:AM 16.9</td>
<td>1.33</td>
<td>+ 2 days</td>
</tr>
<tr>
<td>PM Vitreous Humor</td>
<td>11.33</td>
<td>0.39</td>
<td>PM:AM 28.9</td>
<td>3.9</td>
<td>+ 2 days</td>
</tr>
</tbody>
</table>

Figure 1. "Ecstasy" tablet seized/analysed during hospital admission. Contents found to be paracetamol, MDA, ketamine and amphetamine.

Analytical Methods
MDMA and MDA quantitative analysis was performed using high performance liquid chromatography with diode-array UV detection (HPLC-DAD). 500 μl of internal standard (5 mg/L norfenfluramine or 2 mg/L cinchonine in 0.2M NaSO4) was added to 500 μl of sample and extracted with 5 mL of 1-chlorobutane and back extracted into 100 μl of 0.8M H2O. Chromatography was based on a Waters 5 micron OD/CN column and a 210 nm was used as the detection wavelength. A linear calibration range of 0.1 to 5 mg/L (MDMA) and 0.05 to 2.5 mg/L (MDA) was produced using blank (pre-screened) equine plasma. Inter-laboratory precision was determined using internal quality control standards (0.5 mg/L, 1 mg/L, 2 mg/L, 4 mg/L, (MDMA) and 0.1 mg/L and 1 mg/L MDA). Mean concentrations of 0.20 mg/L, 1.96 mg/L (MDMA) and 0.11 mg/L, 1.04 mg/L (MDA) were calculated (n=10). Limit of detection was 0.01 mg/L.

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