Behavioral Health is Essential To Health
Prevention Works
Treatment is Effective
People Recover
Oxycodone and Hydrocodone: Detection in Urine, Oral Fluid, and Blood

Division of Workplace Programs, SAMHSA

June 10, 2014
Research Studies

Oxycodone and Hydrocodone: Kinetic Relationships of Whole Blood to Oral Fluid
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Disposition of Oxycodone and Hydrocodone in Oral Fluid
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Prescription Opioids. I. Profiling Oxycodone and Metabolites in Urine
Ronald R. Flegel*, Charles P. LoDico1, Rebecca Heltsley2, David L. Black2,3, John M. Mitchell4, and Edward J. Cone5

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Prescription Opioid Abuse. II. Profiling Hydrocodone and Metabolites in Urine
Charles P. LoDico1, Ronald R. Flegel1, Rebecca Heltsley2, David L. Black2,3, John M. Mitchell4, and Edward J. Cone5

1Substance Abuse and Mental Health Services Administration, Division of Workplace Programs, Rockville, MD, USA; 2Aegis Sciences Corporation, 515 Great Circle Road, Nashville, TN, USA; 3Vanderbilt University, Department of Pathology, Immunology and Microbiology Nashville, TN, USA; 4RTI International, Research Triangle Park, NC, USA; 5Johns Hopkins School of Medicine, Baltimore, MD, USA
• Study details
• Review of oxycodone and hydrocodone controlled clinical study results
• Examination of close relationship between oral fluid and blood
• Summary of the detection of metabolites in urine
Introduction

• Illicit prescription opioid use is now more prevalent in the US than the combined use of heroin, cocaine and methamphetamine.

• The US is the world’s largest consumer of oxycodone (OC) per capita. The combination product, hydrocodone (HC) with acetaminophen, is the most frequently prescribed opioid drug in the U.S.

• OC, HC, and other semi-synthetic opioids have become the most commonly misused prescription drugs in the U.S.

• Currently, OC and HC are not tested in US federal workplace programs, but there is considerable interest in adding them and other semi-synthetic opiate analgesics (i.e., oxycodone, oxymorphone, hydrocodone, hydromorphone) to the test panel because of their widespread abuse and impairing effects.
Study Overview

- Conduct a dosing study under IRB approval and informed consent with healthy, drug-free volunteers
- Characterize the time course of appearance and disappearance of oxycodone and hydrocodone
  - Oral fluid
  - Blood
  - Urine
Study Goals

• **Oxycodone and Hydrocodone: Kinetic Relationships of Whole Blood to Oral Fluid**
  Goal: Establish the core information on the distribution pattern of OC and HC in blood and Oral Fluid

• **Disposition of Oxycodone and Hydrocodone in Oral Fluid**
  Goal: Evaluate the kinetics and disposition of OC and HC in Oral Fluid. Determine the strength of correlation between OF and blood

• **Prescription Opioids. I. Profiling Oxycodone and Metabolites in Urine**
  Goal: Delineate the time course of OC and metabolites in human urine following controlled administration with a single 20 mg oral dose of OC hydrochloride

• **Prescription Opioids. II. Profiling Hydrocodone and Metabolites in Urine**
  Goal: Delineate the time course of HC and metabolites in human urine following controlled administration with a single 20 mg oral dose of HC bitartrate
Study Dosing Information

• Oxycodone
  • Single dose, one OxyContin® tablet, 20 mg oxycodone HCl (total = 17.9 mg OC)

• Hydrocodone
  • Single dose, two Norco® tablets, each containing 10 mg hydrocodone bitartrate (total =12.1 mg HC) and 325 mg acetaminophen
  • 20 mg HC bitartrate (12.1 mg HC)
Study Design

• Single center, randomized, parallel group, open-label, single dose study
• 12 Subjects per drug group
• Healthy adult volunteers
• Drug-free
• Timed oral fluid and blood collections
• Pooled urine specimens
• Two nights residence on controlled clinical ward
Subjects

- Oxycodone group (n=12)
  - 7M/5F
  - Mean age (range): 31.5 (20-44) yr
  - Mean weight: 76.7 (56.7-92.8) kg
  - Ethnicity: 8 B, 2 W, 1 H, 1 Multi

- Hydrocodone group (n=12)
  - 7M/5F
  - Mean age (range): 33.9 (24-44) yr
  - Mean weight: 76.8 (49.0-100.0) kg
  - Ethnicity: 10 B, 1 W, 1 Multi
Study Timeline & Specimen Collection

OFF: -1, 0.25, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 14, 24, 28, 32, 36, 48, 49, 50, 52

BL: -1, 0.25, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 14, 24, 28, 32, 36, 48, 52

UR: -1, 0-2, 2-4, 4-6, 6-8, 8-10, 10-12, 12-14, 14-24, 24-28, 28-32, 32-36, 48-52

Day -13 to Day -1
Testing
Screening
Informed Consent

Day -1
Clinic Admission
Drug test

Day 1
Dose “Zero hour” Collection

Day 2 Continue Collection

Day 3 Continue Collection
48-52
Discharge @52 hr
Specimens

• Oral fluid
  • Expectoration, up to 5 min, 15 mL plastic cent tubes, stored frozen

• Whole blood
  • 10 mL by venipuncture, vacutainer (gray top), separated into two aliquots, cryotubes, stored frozen

• Urine
  • Pooled specimens, empty bladder at timed intervals, measure total volume, save two 30 mL aliquots in separate bottles, stored frozen
Analytical Methods

- LC-MS-MS (ABSCIEX 3200) validated method
- Specimens analyzed for 12 opioid analytes (OC, OM, NOC, NOM, HC, HM, HNC, DHC, COD, MOR, NCOD, NMOR)
- Blood LOD = 5 ng/mL for all analytes
- Oral fluid LOD = 1 ng/mL (N/A for NMOR and NOM)
- Urine: Analyzed for “total” (hydrolyzed) and free (non-hydrolyzed)
- Urine LOD: 50 ng/mL for all analytes except NOM (100 ng/mL)
- Urine: Creatinine & specific gravity
Review of Oxycodone Metabolism
(Urine, Oral Fluid and Blood)

Oxycodone (OC) → Noroxycodone (NOC) via CYP3A4

Oxymorphone (OM) → Noroxymorphone (NOM) via CYP2D6
Review of Hydrocodone Metabolism
(Urine, Blood, & Oral Fluid)

Hydrocodone (HC) → CYP3A4 → Norhydrocodone (NHC)

Hydromorphone (HM) → CYP2D6

Dihydrocodeine (DHC) → 6-Ketoreductase
Results: Adverse Events

- No serious AEs
- Mild to moderate: OC, 8 (4M/4F); HC, 6 (2M/4F)
  - Nausea: OC, 5; HC 6
  - Vomiting: OC, 4; HC 3
  - Lightheadedness: OC, 4; HC, 4
  - Itching: OC, 2; HC, 1
- Other minor reports: antecubital soreness, irritability, shaky, and feeling high
Blood and Oral Fluid Results
Oxycodone and Hydrocodone: Comparison of Oral Fluid to Blood

Graph showing the concentration of oxycodone and hydrocodone in oral fluid and blood over time.
Noroxycodone & Norhydrocodone
Comparison of Oral Fluid to Blood

- NOC BL Mean
- NOC OF Mean

ng/mL vs Hours for Noroxycodone (NOC)

- NHC BL Mean
- NHC OF Mean

ng/mL vs Hours for Norhydrocodone (NHC)
# Cmax, OF/BL Ratios, Correlations

## Oxycodone

<table>
<thead>
<tr>
<th></th>
<th>OC</th>
<th>NOC</th>
<th>OM</th>
<th>NOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>OF Cmax (N)</td>
<td>132.7 (12)</td>
<td>18.7 (12)</td>
<td>1.6 (7)</td>
<td>ND</td>
</tr>
<tr>
<td>BL Cmax (N)</td>
<td>20.6 (12)</td>
<td>15.6 (12)</td>
<td>ND</td>
<td>6.4 (6)</td>
</tr>
<tr>
<td>OF/BL Ratio</td>
<td>5.4 (12)</td>
<td>1.0 (12)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>OF:BL, r</td>
<td>0.719 (12)</td>
<td>0.651 (12)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

## Hydrocodone

<table>
<thead>
<tr>
<th></th>
<th>HC</th>
<th>NHC</th>
<th>HM</th>
<th>DHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>OF Cmax (N)</td>
<td>207.7 (12)</td>
<td>12.8 (12)</td>
<td>ND</td>
<td>6.4 (12)</td>
</tr>
<tr>
<td>BL Cmax (N)</td>
<td>49.3 (12)</td>
<td>18.7 (11)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>OF/BL Ratio</td>
<td>3.2 (12)</td>
<td>0.7 (11)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>OF:BL, r</td>
<td>0.733 (12)</td>
<td>0.423 (11)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
Oxycodone Correlation

OC 10

\[ y = 3.7036x + 0.0682 \]

\[ R^2 = 0.932 \]

OC 24

\[ y = 5.1418x + 28.798 \]

\[ R^2 = 0.1427 \]
Hydrocodone Correlation

**HC 12**

\[ y = 3.1587x - 19.755 \]
\[ R^2 = 0.8376 \]

**HC 13**

\[ y = 2.156x + 1.1595 \]
\[ R^2 = 0.1719 \]
<table>
<thead>
<tr>
<th>Kinetic Parameter</th>
<th>Oxycodone</th>
<th>Hydrocodone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral fluid $T_{1/2}$, hr (N)</td>
<td>4.6 (12)</td>
<td>8.3 (12)</td>
</tr>
<tr>
<td>Blood $T_{1/2}$, hr (N)</td>
<td>5.6 (11)</td>
<td>11.8 (11)</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>NHC</td>
</tr>
<tr>
<td></td>
<td>4.4 (12)</td>
<td>6.2 (9)</td>
</tr>
<tr>
<td></td>
<td>4.5 (12)</td>
<td>7.7 (11)</td>
</tr>
</tbody>
</table>
Summary of Blood and Oral Fluid

- OC and HC appeared in OF and BL within 15-30 minutes after oral administration.
- Because OC was an extended release preparation, entry into oral fluid was slower and concentrations remained elevated longer relative to HC.
- The profile of appearance and disappearance was similar but analytes were detected for longer times in OF.
- OF concentrations were considerably higher for parent drug in OF compared to urine.
- Normetabolite concentrations were similar in OF and BL.
- Kinetic parameters were similar.
- Correlations were high but not predictive.
- Notably, O-demethylated metabolites (OM, HM) were in low or non-detectable concentrations.
- The N-demethylated metabolites were present at similar times as the parent drug but were generally in lower concentrations.
- A pilot study of blood hydrolysis (n=2) revealed somewhat higher concentrations of OM (data not shown).
Urine Results
OC and NOC generally became detectable in the 0-2 h collection period. OM generally became detectable in the 2-4 h collection period. 

- OC and its metabolite concentrations usually peaked within 3–9 h, then declined. 
- After 24 hours, 18 specimens contained detectable concentrations of both OM and NOC, with no OC. 
- Generally, total concentrations of OC and NOC were similar to free concentrations. 
- Total OM concentrations were substantially greater than free concentrations. 
- Total NOM concentrations were slightly higher than free concentrations. 

- Total HM and DHC generally became detectable in the 2-4 h collection period. 
- HC and metabolites’ concentrations peaked within 3-9 h post-dosing, then declined.
Variability of HC Excretion in Urine (Hydrolyzed)

HC was present in 9 of 12 subjects’ specimens from the first collection period (0-2 h).
Oxycodone: Mean Detection Times
Total OC, OM, NOC and NOM in Urine (Time to last Positive by Cutoff)

- Mean detection times for NOC were 5 to 12.5 hours longer than mean OC detection times at all cutoffs.
- Using cutoffs up to 2000 ng/mL, mean detection times for OM were 1 to 12 hours longer than mean OC detection times. However, using the 2000 ng/mL cutoff, the mean detection time for OC was 0.7 h longer than the mean OM detection time.
Hydrocodone: Mean Detection Times
Total HC, HM, NHC and DHC in Urine, Time to last Positive by Cutoff

- Mean detection times for NHC were 1.7 to 12.5 hours longer than mean HC detection times at all cutoffs.
- Mean detection times of HC were longer than mean HM and DHC detection times at all cutoffs.
The combination of OC, OM, and NOC identified the largest number of specimens at each cutoff evaluated.

Of the single analytes, NOC identified the largest number of specimens at each cutoff evaluated.

Of the single analytes, NHC identified the largest number of specimens at each cutoff evaluated.

Monitoring HC and HM only would decrease the number of specimens identified.

*Total analyte concentrations after hydrolysis
### Oxycodone: Cutoff Evaluation by Analyte

#### Percentage of Specimens Containing Analytes at or above Cutoff

<table>
<thead>
<tr>
<th>Cutoff (ng/mL)</th>
<th>OC</th>
<th>OM</th>
<th>NOC</th>
<th>OC/OM</th>
<th>OM/NOC</th>
<th>OC/OM/NOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>81</td>
<td>87</td>
<td>97</td>
<td>98</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>100</td>
<td>77</td>
<td>93</td>
<td>98</td>
<td>97</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>150</td>
<td>75</td>
<td>95</td>
<td>98</td>
<td>96</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>300</td>
<td>74</td>
<td>85</td>
<td>100</td>
<td>92</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>500</td>
<td>60</td>
<td>61</td>
<td>97</td>
<td>70</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>1000</td>
<td>38</td>
<td>25</td>
<td>100</td>
<td>42</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>2000</td>
<td>35</td>
<td>30</td>
<td>100</td>
<td>35</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

- Monitoring OC and OM identified 98% of specimens at a cutoff of 50 ng/mL, 97% at 100 ng/mL, 96% at 150 ng/mL, and 92% at 300 ng/mL.
- Higher percentages of specimens were identified by monitoring NOC in addition to OC and OM at cutoffs greater than 300 ng/mL.
### Hydrocodone: Cutoff Evaluation by Analyte
Percentage of Specimens Containing Analytes at or above Cutoff

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>HC</th>
<th>HM</th>
<th>DHC</th>
<th>HC/HM</th>
<th>NHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>79</td>
<td>65</td>
<td>40</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>100</td>
<td>75</td>
<td>39</td>
<td>21</td>
<td>81</td>
<td>100</td>
</tr>
<tr>
<td>150</td>
<td>75</td>
<td>35</td>
<td>13</td>
<td>78</td>
<td>100</td>
</tr>
<tr>
<td>300</td>
<td>65</td>
<td>21</td>
<td>5</td>
<td>66</td>
<td>100</td>
</tr>
<tr>
<td>500</td>
<td>55</td>
<td>12</td>
<td>0</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>1000</td>
<td>45</td>
<td>3</td>
<td>0</td>
<td>45</td>
<td>100</td>
</tr>
<tr>
<td>2000</td>
<td>53</td>
<td>0</td>
<td>0</td>
<td>53</td>
<td>100</td>
</tr>
</tbody>
</table>

- Monitoring HC and HM identified 86% of specimens at a cutoff of 50 ng/mL and 81% at 100 ng/mL.
- Higher percentages of specimens were identified by monitoring NHC alone or in addition to HC and HM at all cutoffs.
### Number of Specimens with OC or OC and Metabolites at or above 50 ng/mL, by Collection Period

<table>
<thead>
<tr>
<th>Coll. Period (h)</th>
<th>n</th>
<th>OC</th>
<th>OC/OM</th>
<th>OM/NOC</th>
<th>OC/OM/NOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>12</td>
<td>11</td>
<td>11</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>2-4</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>4-6</td>
<td>10</td>
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<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>6-8</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>8-10</td>
<td>12</td>
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<tr>
<td>10-12</td>
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<td>12</td>
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<tr>
<td>12-14</td>
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<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
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<tr>
<td>14-24</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
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<tr>
<td>24-28</td>
<td>12</td>
<td>9</td>
<td>11</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>28-32</td>
<td>12</td>
<td>4</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>32-36</td>
<td>12</td>
<td>2</td>
<td>10</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>48-52</td>
<td>12</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>137</td>
<td>103</td>
<td>125</td>
<td>125</td>
<td>127</td>
</tr>
</tbody>
</table>

- After 24 hours, additional specimens were identified by monitoring OM in addition to OC.
- After 24 hours, 2 additional specimens were identified by monitoring NOC in addition to OC and OM.
- OC alone was detected in 2 specimens from the 0-2 h collection period. Thereafter, monitoring NOC and OM was as effective in detecting OC use as monitoring OC, NOC, and OM.
### Number of Specimens with HC or HC and Metabolites at or above 50 ng/mL, by Collection Period

<table>
<thead>
<tr>
<th>Coll. Period (h)</th>
<th>n</th>
<th>HC</th>
<th>HC/HM</th>
<th>HC/HM/NHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>10</td>
<td>9</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>2-4</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>4-6</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>6-8</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>8-10</td>
<td>12</td>
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<td>10-12</td>
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<td>12-14</td>
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<tr>
<td>14-24</td>
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</tr>
<tr>
<td>28-32</td>
<td>12</td>
<td>1</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>32-36</td>
<td>12</td>
<td>1</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>48-52</td>
<td>12</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>139</td>
<td>100</td>
<td>108</td>
<td>126</td>
</tr>
</tbody>
</table>

- After 28 hours, 8 additional specimens were identified by monitoring HM in addition to HC.
- 18 additional specimens were identified by monitoring NHC in addition to HC and HM. 17 of these additional specimens were identified after 24 hours.
Hydrocodone: Mean Maximum Urine Concentration, Time to Maximum Concentration, and the Percent Dose Excreted in Urine over 36 h following Dosing

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Cmax ± SEM (Range), ng/mL</th>
<th>Tmax ± SEM (Range), hrs</th>
<th>% Dose Excreted ± SEM (Range), 0-36 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC (Total)</td>
<td>12</td>
<td>2036 ± 588 (577 - 5626)</td>
<td>3.5 ± 1.0 (3.0 - 7.0)</td>
<td>9.0 ± 1.0 (2.7 - 13.5)</td>
</tr>
<tr>
<td>HC (Free)</td>
<td>12</td>
<td>1981 ± 572 (521 - 4160)</td>
<td>3.5 ± 1.0 (3.0 - 7.0)</td>
<td>9.2 ± 1.4 (1.9 - 16.1)</td>
</tr>
<tr>
<td>HM (Total)</td>
<td>11</td>
<td>443 ± 134 (78 - 1285)</td>
<td>3.5 ± 1.1 (3.0 - 7.0)</td>
<td>2.1 ± 0.5 (0.0 - 4.9)</td>
</tr>
<tr>
<td>HM (Free)</td>
<td>7</td>
<td>110 ± 42 (54 - 268)</td>
<td>3.3 ± 1.2 (3.0 - 5.0)</td>
<td>0.05 ± 0.02 (0.0 - 0.2)</td>
</tr>
<tr>
<td>NHC (Total)</td>
<td>12</td>
<td>3020 ± 872 (867 - 8617)</td>
<td>3.7 ± 1.1 (3.0 - 7.0)</td>
<td>19.2 ± 2.2 (8.9 - 29.8)</td>
</tr>
<tr>
<td>NHC (Free)</td>
<td>12</td>
<td>3007 ± 868 (881 - 7673)</td>
<td>3.7 ± 1.1 (3.0 - 7.0)</td>
<td>19.7 ± 2.5 (7.9 - 32.9)</td>
</tr>
<tr>
<td>DHC (Total)</td>
<td>11</td>
<td>190 ± 57 (61 - 364)</td>
<td>4.8 ± 1.5 (3.0 - 9.0)</td>
<td>0.7 ± 0.2 (0.0 - 2.0)</td>
</tr>
<tr>
<td>DHC (Free)</td>
<td>10</td>
<td>193 ± 61 (71 - 384)</td>
<td>4.4 ± 1.4 (3.0 - 9.0)</td>
<td>0.5 ± 0.1 (0.0 - 1.8)</td>
</tr>
<tr>
<td>Total Dose (Total)</td>
<td>12</td>
<td>NA</td>
<td>NA</td>
<td>31.1 ± 3.0 (13.7 - 41.1)</td>
</tr>
<tr>
<td>Total Dose (Free)</td>
<td>10</td>
<td>NA</td>
<td>NA</td>
<td>29.4 ± 3.7 (10.1 - 48.2)</td>
</tr>
</tbody>
</table>

Abbreviations: Cmax, maximum urine concentration; Tmax, time to maximum urine concentration; SEM, standard error of mean; Hyd, hydrolyzed; NA, not applicable

- Approximately 30 percent of the oral dose was excreted in the urine as HC, HM, NHC and DHC during the 52 hours of observation.
- Approximately two thirds of the dose was excreted as NHC
Results Overview: Oxycodone and Hydrocodone

**Oxycodone**
- All BL specimens (immediately before OC dosing) were negative (less than LOQ) for all analytes.
- OC was detected in specimens from the first collection period (0–2 h) for 11 of the 12 subjects.
- The initial appearance of OC was frequently accompanied by NOC in the same specimen.
- NOC was generally the most abundant metabolite and was frequently present in higher concentrations than OC.

**Hydrocodone**
- HC and NHC were initially detected in the majority of subjects’ specimens within 2 hours of drug administration. HC was most frequently detected in combination with NHC.
- NHC was the most abundant metabolite and was often present in higher concentration than HC.
Summary
Oxycodone in Urine

- The 12 subjects exhibited considerable variability in the excretion of OC and metabolites. OC and NOC were initially detected in the majority of subject specimens within 2 hours of drug administration.

- Cutoffs of 50, 100, or 150 ng/mL gave detection times for OC, OM, NOC, and NOM of 24 h or greater.

- Hydrolyzed versus unhydrolyzed results showed that OC and NOC were excreted nearly completely in the unconjugated form, while OM was excreted mostly in the conjugated form.

- **Overall, these data suggest that monitoring OC and OM would be effective at cutoffs up to 300 ng/mL.**

- Some consideration should be given to the inclusion of NOC as a routine confirmatory test analyte, or alternately, as a special test to assist in results interpretation (e.g., OC versus OM use).
Summary
Hydrocodone in Urine

• Hydrolyzed versus non-hydrolyzed results indicated that HC, NHC, and DHC were excreted nearly completely in the unconjugated form, and HM was excreted primarily in the conjugated form.

• Detection times for HC and metabolites were less than 5 h using a 2000 ng/mL cutoff concentration. Use of a 50 ng/mL cutoff concentration extended detection time for HC to approximately 28 h.

• Overall, these data suggest that drug testing requirements for HC should include tests for HC and HM in hydrolyzed urine.

• Some consideration should also be given to allowing testing for NHC as a routine confirmatory test analyte or alternately, as a special test to assist in results interpretation (i.e., to distinguish HC from HM use).
Thank You

Division of Workplace Programs

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