Emerging Designer Drug Monograph

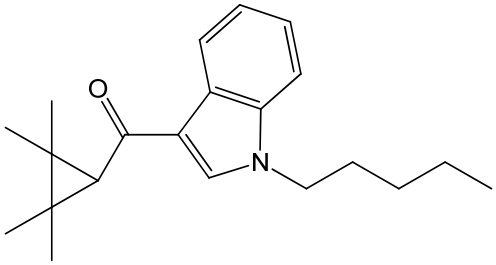
Date: November 4, 2013

Author(s): Gregory W. Endres, Sumandeep Rana

Drug Name: **UR-144**

Synonyms: KM-X1

Structure:



Formula: $C_{21}H_{29}NO$

Molecular Weight: 311.5

Pharmacological Drug Class: Synthetic cannabinoid, dual CB1/CB2 agonist.

Metabolism: *In vitro* metabolism of the 5-fluoro analog of UR-144, XLR-11, was investigated by incubating XLR-11 in human hepatocytes (1). Based on structural similarity between UR-144 and XLR-11 and the known metabolites of JWH 018 and AM2201 (2), the analogous naphthoyl structures, it would be reasonable to predict the presence of common omega-hydroxy and omega-carboxy metabolites. However, it was also reported that the cyclopropyl ring-opened thermal degradation product (3) is in higher concentration than UR-144 and XLR-11 in pyrolysis studies (4, 5), therefore metabolic studies of pure XLR-11 may not fully represent the *in vivo* metabolites where the mode of delivery is smoking.

Blood Concentrations: There are no published reports on blood concentrations.

Effects and Toxicity: UR-144 is a potent synthetic cannabinoid designed by Abbott Laboratories as a CB2 selective agonist for pain management and other indications (6). UR-144 preferentially binds the peripheral CB_2 receptor (K_i = 1.8 nM) over the central CB_1 receptor (K_i = 150 nM) (7, 8). In drug discrimination studies in mice, UR-144 generalized to Δ9-THC as well as JWH018 and *in vitro* studies show it binds to CB1 similarly to JWH 018 and AM2201 (9).

Analysis: Based on user reports and crime lab statistics UR-144 is predominantly smoked as an adulterant in "herbal smoking mixtures; aka K2/spice. UR-144 and the 5-fluoro analog, XLR-11, become a widely abused synthetic cannabinoid in spice/K2 herbal mixtures beginning in early 2012 and have been linked to acute kidney injury. Analytical data are available in the references cited in the Forendex database (10), SWGDRUG (11), and Forensic Drug Review monographs (3).

References:

1. Wohlfarth, A., Panq, S., Zhu, M., Gandhi, A.S., Scheidweiler, K.B, Liu, H.F., *et al*. (2013) First metabolic profile of XLR-11, a novel synthetic cannabinoid, obtained by using human hepatocytes and high-resolution mass spectrometry. *Clinical Chemistry*, **59:11**, 1638-1648. http://www.ncbi.nlm.nih.gov/pubmed/24014837

2. Chimalakonda, K.C., Seely, K.A., Brattton, S.M., Brents, L.K., Moran, C.L., Endres, G.W., *et al*. (2012) Cytochrome P450-mediated oxidative metabolism of abused synthetic cannabinoids found in K2/Spice: identification of novel cannabinoid receptor ligands. *Drug Metabolism and Disposition*, **40(11)**, 2174-2184. http://www.ncbi.nlm.nih.gov/pubmed/22904561

3. Kennedy, P. D, Endres, G.W., Deakin, A., Eckre, D. (2012) Characterization of the thermal degradation product of UR-144. *Forensic Drug Review Monograph.* http://www.forensicdrugreview.com/

4. Rana, S. (Oct. 30, 2013) Monitoring oral fluid for pyrolysis products of XLR-11 and UR-144 as an indication of XLR-11 and UR-144 ingestion. SOFT annual conference, oral presentation.

5. Thomas, B. (29 June 2006) Analysis of smoke condensate from herbal cigarettesl with fluorinated synthetic cannabinoids. SOFT annual conference, oral presentation.

6. Pace, J.M., Tietje, K., Dart, M.J., Meyer, M.D. (2006) 3-Cycloalkylcarbonyl indoles as cannabinoid receptor ligands. WO/2006/069196 A1. http://patentscope.wipo.int/search/en/WO2006069196

7. Frost, J.M., Dart, M.J., Tietje, K.R., Garrison, T.R., Grayson, G.K., Daza, A.V., El-Kouhen, O.F., *et al*. (2010) Indol-3-ylcycloalkyl ketones: effects of N1 substituted indole side chain variations on CB2 cannabinoid receptor activity. *Journal of Medical Chemistry*, **53**, 295-315. http://www.ncbi.nlm.nih.gov/pubmed/19921781

8. Murphy, T.D. (2013) Acute kidney injury associated with synthetc cannabinoid use- muliple states, 2012. *Morbidity and Mortality Weekly Report*, **62(6)**, 93-98. http://www.ncbi.nlm.nih.gov/pubmed/23407124

9. (2013) UR-144 (TCMP-018; KM-X1) and XLR11 (5-F-UR-144). Drug Enforcement Administration, Office of Diversion Control, *Drug & Chemical Evaluation Section.* http://www.deadiversion.usdoj.gov/drug_chem_info/spice/spice_ur144_xlr11.pdf

10. Ur-144. Southern Association of Forensic Scientists. http://forendex.southernforensic.org/index.php/detail/index/1218

11. UR-144. Drug Enforcement Administration. http://www.swgdrug.org/Monographs/UR144.pdf