Emerging Designer Drug Monograph

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Drug Name: AM-2201, see also JWH-018 (one of AM-2201's metabolites)

Synonyms: [1-(5-fluoropentyl)-1H-indol-3-yl]-1-naphthalenyl-methanone

CAS#: 335161-24-5

Structure:

N F

Formula: C₂₄H₂₂FNO

Molecular Weight: 359.4

Pharmacological Drug Class: Cannabinoid, naphthoylalkylindole class. AM-2201 is a potent but nonselective full agonist for the cannabinoid receptor. Affinities are with a K_i of 1.0nM at CB_1 and 2.6nM at CB_2 (1).

Metabolism: Numerous metabolism products have been identified (1-7). These include: AM-2201 4-Hydroxypentyl Glucuronide, JWH-018 5-Hydroxypentyl Glucuronide, JWH-018 N-Pentanoic Acid, JWH-018 N-Propionic Acid, and JWH-073 N-Butanoic Acid and AM-2201 6-hydroxyindole. Many of these metabolites are in common with JWH-018 metabolites.

Blood Concentrations: Blood levels in one DUID study from Norway were reported as less than 0.5 ng/g (8). Logan and Yeakel reported results from a US study where results were 0.43-4.0 ng/mL (9). Other reports have reported similar levels (10-13).

Effects and Toxicity: Anecdotal reports of panic attacks and vomiting at doses as low as 2 mg. Convulsions may occur at doses over 10 mg (14). AM-2201 may be active at doses as low as 500 ug. It has a very steep dose-response curve and tolerance builds up quickly. There is a high potential for overdose and withdrawal symptoms. Due to batch variability there may be significant difference in effects (14-16). In one case, AM-2201 was found in the blood of a person who died from a stab wound to the neck (17).

Analysis: This drug in blood and serum (8-13), hair (18), oral fluid (19-21), and herbal mixtures (22-28). Metabolites of this drug have been detected in urine (29-31).

This is a simple neutral drug, with a low molecular. Analytical data are available in the references cited in the Forendex database and on SWGDRUG monographs.

References:

- 1. Chimalakonda, K.C., Seely, K.A., Bratton, 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
- 2. Lovett, D.P., Yanes, E.G., Herbelin, T.W., Knoerzer, T.A., Levisky, J.A. (2013) Structure elucidation and identification of a common metabolite for naphthoylindole-based synthetic cannabinoids using LC-TOF and comparison to a synthetic reference standard. *Forensic Science International*, 226(1-3), 81–87. http://www.ncbi.nlm.nih.gov/pubmed/23313601
- 3. Hutter, M., Moosmann, B., Kneisel, S., Auwärter, V. (2013) Characteristics of the designer drug and synthetic cannabinoid receptor agonist AM-2201 regarding its chemistry and metabolism. *Journal of Mass Spectrometry*, **48**(7), 885-894. http://onlinelibrary.wiley.com/doi/10.1002/jms.3229/pdf
- 4. Sobolevsky, T., Prasolov, I., Rodchenkov, G. (2012) Detection of urinary metabolites of AM-2201 and UR-144, two novel synthetic cannabinoids. *Drug Testing and Analysis*. http://www.ncbi.nlm.nih.gov/pubmed/23042760
- Patton, A.L., Seely, K.A., Chimalakonda, K.C., Tran, J.P., Trass, M., Miranda, A., et al. (2013) Targeted metabolomic approach for assessing human synthetic cannabinoid exposure and pharmacology. *Analytical Chemistry*, 85(19), 9390-9399. http://pubs.acs.org/doi/pdf/10.1021/ac4024704
- 6. Stout, S.M., Cimino, N.M. (2013) Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. *Drug Metabolism Reviews*. http://www.ncbi.nlm.nih.gov/pubmed/24160757
- Donohue, K.M., Steiner, R.R. (2012) JWH-018 and JWH-022 as Combustion Products of AM2201. *Microgram Journal*, 9(2), 52-56. http://www.justice.gov/dea/pr/microgram-journals/2012/mi9 52-56.pdf
- 8. Tuv, S.S., Krabseth, H., Karinen, R., Olsen, K.M., Oiestad, E.L., Vindenes, V. (2013) Prevalence of synthetic cannabinoids in blood samples from Norwegian drivers suspected of impaired driving during a seven weeks period. *Accidental Analysis and Prevention*, **62C**, 26-31. http://www.sciencedirect.com/science/article/pii/S000145751300362X
- 9. Yeakel, J.K., Logan, B.K. (2013) Blood synthetic cannabinoid concentrations in cases of suspected impaired driving. *Journal of Analytical Toxicology*, **37(8)**, 547-551. http://www.ncbi.nlm.nih.gov/pubmed/23965292
- 10. Musshoff, F., Madea, B., Kernbach-Wighton, G., Bicker, W., Kneisel, S., Hutter, M., Auwärter, V. (2013) Driving under the influence of synthetic cannabinoids ("Spice"): a case series. *International Journal of Legal Medicine*. http://www.ncbi.nlm.nih.gov/pubmed/23636569

- 11. Kronstrand, R., Roman, M., Andersson, M., Eklund, A. (2013) Toxicological findings of synthetic cannabinoids in recreational users. *Journal of Analytical Toxicology*, **37(8)**, 534-541. http://www.ncbi.nlm.nih.gov/pubmed/23970540
- 12. Wikström, M., Thelander, G., Dahlgren, M., Kronstrand, R. (2013) An accidental fatal intoxication with methoxetamine. Journal of Analytical Toxicology, **37(1)**, 43-46. http://www.ncbi.nlm.nih.gov/pubmed/23111916
- 13. Kneisel, S., Auwärter, V. (2012) Analysis of 30 synthetic cannabinoids in serum by liquid chromatography-electrospray ionization tandem mass spectrometry after liquid-liquid extraction. Journal of Mass Spectrometry, 47(7), 825-835. http://www.ncbi.nlm.nih.gov/pubmed/22791249

Effects and Toxicity

- 14. McQuade, D., Hudson, S., Dargan, P.I., Wood, D.M. (2013) First European case of convulsions related to analytically confirmed use of the synthetic cannabinoid receptor agonist AM-2201. *European Journal of Clinical Pharmacology*, 69(3), 373-376. http://www.ncbi.nlm.nih.gov/pubmed/22936123
- 15. Tomiyama, K.I., Funada, M. (2013) Cytotoxicity of synthetic cannabinoids on primary neuronal cells of the forebrain: the involvement of cannabinoid CB(1) receptors and apoptotic cell death. *Toxicology and Applied Pharmacology*. http://www.ncbi.nlm.nih.gov/pubmed/24211273
- Hopkins, C.Y., Gilchrist, B.L. (2013) A case of cannabinoid hyperemesis syndrome caused by synthetic cannabinoids. Journal of Emergency Medicine, 45(4), 544-546. http://www.ncbi.nlm.nih.gov/pubmed/23890687
- 17. Patton, A.L., Chimalakonda, K.C., Moran, C.L., McCain, K.R., Radominska-Pandya, A., James, L.P., *et al.* (2013) K2 toxicity: fatal case of psychiatric complications following AM2201 exposure. *Journal of Forensic Sciences*, **58(6)**, 1676-1680. http://www.ncbi.nlm.nih.gov/pubmed/23822805

Hair

18. Hutter, M., Kneisel, S., Auwärter, V., Neukamm, M.A. (2012) Determination of 22 synthetic cannabinoids in human hair by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography B Analytical Technologies in the Biomedical and Life Sciences*, **903**, 95-101. http://www.ncbi.nlm.nih.gov/pubmed/22835826

Oral Fluid

- 19. Oiestad, E.L., Johansen, U., Christophersen, A.S., Karinen, R. (2013) Screening of synthetic cannabinoids in preserved oral fluid by UPLC-MS/MS. *Bioanalysis*, **5(18)**, 2257-2268. http://www.ncbi.nlm.nih.gov/pubmed/24053241
- Rodrigues, W.C., Catbagan, P., Rana, S., Wang, G., Moore, C. (2013) Detection of synthetic cannabinoids in oral fluid using ELISA and LC-MS-MS. *Journal of Analytical Toxicology*, 37(8), 526-533. http://www.ncbi.nlm.nih.gov/pubmed/23946452

21. Kneisel, S., Auwärter, V., Kempf, J. (2012) Analysis of 30 synthetic cannabinoids in oral fluid using liquid chromatography-electrospray ionization tandem mass spectrometry. *Drug Testing and Analysis*, **5**, 657-669. http://www.ncbi.nlm.nih.gov/pubmed/23081933

Herbal Mixtures

- 22. Nakajima, J., Takahashi, M., Nonaka, R., Seto, T. Suzuki, J., Yoshida, M., *et al.* (2011) Identification and quantitation of a benzoylindole(2-methoxyphenyl)(1-pentyl-1H-indol-3-yl)methanone and a naphthoylindole 1-(5-fluoropentyl-1H-indol-3-yl)-(naphthalene-1-yl)methanone (AM-2201) found in illegal products obtained via the Internet and their cannabimimetic effects evaluated by in vitro [³⁵S]GTPγS binding assays. *Forensic Toxicology*, **29**, 132-141. http://link.springer.com/article/10.1007%2Fs11419-011-0114-5#
- 23. Langer, N., Lindigkeit, R., Schiebel, H.M., Ernst, L., Beuerle, T. (2014) Identification and quantification of synthetic cannabinoids in 'spice-like' herbal mixtures: A snapshot of the German situation in the autumn of 2012. *Drug Testing and Analysis*, **6**, 59-71. http://www.ncbi.nlm.nih.gov/pubmed/23723183
- Denooz, R., Vanheugen, J.C., Frederich, M., de Tullio, P., Charlier, C. (2013) Identification and structural elucidation of four cannabimimetic compounds (RCS-4, AM-2201, JWH-203 and JWH-210) in seized products. *Journal of Analytical Toxicology*, 37(2), 56-63. http://www.ncbi.nlm.nih.gov/pubmed/23339188
- 25. Uchiyama, N., Kawamura, M., Kikura-Hanajiri, R., Goda, Y. (2013) URB-754: a new class of designer drug and 12 synthetic cannabinoids detected in illegal products. *Forensic Science International*, **227(1-3)**, 21-32. http://www.ncbi.nlm.nih.gov/pubmed/23063179
- 26. Logan, B.K., Reinhold, L.E., Xu, A., Diamond, F.X. (2012) Identification of synthetic cannabinoids in herbal incense blends in the United States. *Journal of Forensic Sciences*, **57**(5), 1168-1180. http://www.ncbi.nlm.nih.gov/pubmed/22834927
- 27. Moosmann, B., Kneisel, S., Girreser, U., Brecht, V., Westphal, F., Auwärter, V. (2012) Separation and structural characterization of the synthetic cannabinoids JWH-412 and 1-[(5-fluoropentyl)-1H-indol-3yl]-(4-methylnaphthalen-1-yl)methanone using GC-MS, NMR analysis and a flash chromatography system. *Forensic Science International*, **220(1-3)**, 17-22. http://www.ncbi.nlm.nih.gov/pubmed/22264627
- Simolka, K., Lindigkeit, R., Schiebel, H.M., Papke, U., Ernst, L., Beuerle, T. (2012) Analysis of synthetic cannabinoids in "spice-like" herbal highs: snapshot of the German market in summer 2011. *Analytical and Bioanalytical Chemistrty*, 404(1), 157-171. http://www.ncbi.nlm.nih.gov/pubmed/22710567

Urine

29. Jang, M., Yang, W., Shin, I., Choi, H., Chang, H., Kim, E. (2013) Determination of AM-2201 metabolites in urine and comparison with JWH-018 abuse. International Journal of Legal Medicine. http://www.ncbi.nlm.nih.gov/pubmed/23884698

- 30. Arntson, A., Ofsa, B., Lancaster, D., Simon, J.R., McMullin, M., Logan, B. (2013) Validation of a novel immunoassay for the detection of synthetic cannabinoids and metabolites in urine specimens. *Journal of Analytical Toxicology*, **37**(5), 284-290.
- 31. Wohlfarth, A., Scheidweiler, K.B., Chen, X., Liu, H.F., Huestis, M.A. (2013) Qualitative confirmation of 9 synthetic cannabinoids and 20 metabolites in human urine using LC-MS/MS and library search. *Analytical Chemistry*, **85**(7), 3730-3738. http://www.ncbi.nlm.nih.gov/pubmed/23458260

SWGDRUG Monograph

http://www.swgdrug.org/Monographs/AM2201.pdf

Forendex Database

http://forendex.southernforensic.org/index.php/detail/index/1097