Emerging Designer Drug Monograph

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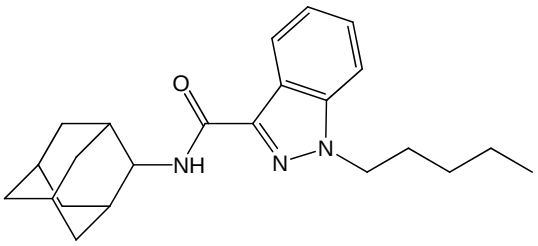
Drug Name: AKB-48

Synonyms: Apinaca**;** 1-pentyl-N-tricyclo -1H-indazole-3-carboxamide

Structure:



Formula: $C_{23}H_{31}N_3O$

Molecular Weight: 365.5

Pharmacological Drug Class: "Synthetic Cannabinoids" of the adamantoylindole class. AKB-48 is related to AB-001 (1-pentyl-3-(1-adamantoyl) indole and AM-1248, which are similar to the JWH series, but the naphthyl ring has been replaced with an adamantly ring.

This class of synthetic cannabinoids is relatively new, generally having appeared after July 2 012, and are sometimes referred to as "3rd generation" synthetic cannabinoids.

AKB-48 is particularly unique in that it contains an amide function adjacent to the adamantly ring and the indole ring present in many of the other synthetic cannabinoids, has been replaced by an indazole ring (1).

Metabolism: AKB-48, the parent compound, is rarely found in urine, but incubation of the parent compound with human hepatocytes did produce 17 novel phase I and II AKB-48 metabolites, including monohydroxylation, dihydroxylation, or trihydroxylation of the aliphatic adamantane ring or N-pentyl side chain. Subsequent glucuronidation of some mono- and di- hydroxylated metabolites also occurred. Due to the inability to detect AKB-48 itself, in urine, AKB-48 ingestion probably will have to be based on finding some of its metabolites in urine at this time.

Oxidation of the N-pentyl side chain which led to the formation of a ketone on the second C from the N, was a minor pathway. Incubation for longer than one hour produces more metabolites after 3 hours. Metabolites were identified by high-resolution mass spectrometry (2).

Blood Concentrations: According to Gandhi and all, no human pharmacokinetic studies have been conducted (2).

Effects and Toxicity: According to Gandhi and all, a KB-48 has twice the affinity for CB-1 receptors as CB-2 receptors (2).

Analysis: AKB-48 is difficult to detect in urine. However hydroxylated metabolites formed following incubation of the parent compound with human hepatocytes, and described above, were identified by high-resolution mass spectrometry (2).

References:

1. Presley, B. C., Janssen-Varnum, S.A., Logan, B. K. (2013) Analysis of synthetic cannabinoids in botanical material: a review of analytical methods and findings. *Forensic Science Review*, **25**, 27-45. http://forendex.southernforensic.org/uploads/references/Presley_Varnum_Logan-_Synthetic_Cannabinoids_in_Botanical_Material.pdf

2. Gandhi, A.S., Zhu, M., Pang, S., Wohlfarth, A., Scheidweiler, K.B., Liu, H.F., *et al*. (2013) First characterization of KB-48 metabolism, a novel synthetic cannabinoid, using human hepatocytes and high-resolution mass spectrometry. *AAPS Journal*, **15(4)**, 1091-1098. http://www.ncbi.nlm.nih.gov/pubmed/23913126