REVIEWING "APINACA", AN EMERGENT SYNTHETIC CANNABINOID RECEPTOR AGONIST

FN. Dinamarca [1], L.Galindo [1,2,4], M. Grifell [1,2], M. Campillo [1], V. Pérez [1,2,4], M.Torrens [1,2,4], M. Farré [2,3,4]

1. Institut de Neuropsiquiatria i Addiccions, Parc de salut mar, Barcelona, Spain.
2. Institut Hospital del Mar d'Investigacions Mèdiques, Barcelona, Spain.
3. Servei de Farmacología Clínica, Hospital Germans Trías i Pujol, Barcelona, Spain
4. Universidad Autónoma de Barcelona, Bellaterra, Spain

Introduction

Since 1990 there is an increase in the synthesis and in some cases the preclinical evaluation of new molecules that act on the cannabinoid synthesis, but no one have been marketed as a medicine. Recently, with the proliferation of New Psychoactive substances (NPS), an important number of synthetic cannabinoid appeared in the "legal high" market as Spice or other names. There is almost no research available and, despite its widespread use, the animal or human pharmacology of substances is unknown.

Objective

Reviewing literature for exposing the history and current state of knowledge of the AKB-48 molecule.

Material and methods

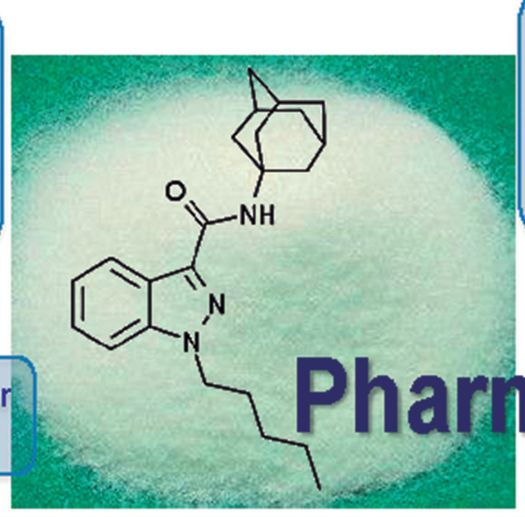
A review of the publications of the molecule is done by searching for keywords "AKB-48" "AKB48" "APINACA" "Synthetic cannabinoids" in Pubmed and Google scholar .

Results - Review

History

The AKB-48, or APINACA, was firstly report in Japanese herbal smoking blends in 2012 (1), nevertheless the origin of the nomination is thought to be in Thailand.

APINACA is clandestinely manufactured. In its pure form is a white powder, soluble in methanol and ethanol, so it can be orally ingested or smoked.



Pharmacology

One of the differences with earlier JHW-type synthetic cannabinoids, is that the molecule has an indazol ring connected to an adamantyl group through a carboxamide linkage (2).

It also has high affinity for the CB2 receptor and somewhat less for the CB1 (3).

The dose needed to produce the desired effect is actually unknown and also have not been described any clinical utility (4). Adarsh S. and colleagues conducted the first characterization of their metabolism in vitro, in a sample of human hepatocytes, describing 17 new metabolites of phases I and II, including glucuronidated metabolites, permitting the identification of the substance in urine analysis for forensic and clinical use (2).

Clinical aspects

The consequences, of using these compounds are unknown, it is presumed that psychosis and dependence are possible, given the similarities with marijuana. Synthetic cannabinoids intoxication, like the overuse of THC, can cause tachycardia, hypertension, nausea, vomiting, drowsiness, hallucinations and acute psychotic reactions (5).

Specifically regarding this molecule, it has been described the potential genotoxic properties of alkylindazoles and aminoalkyl indoles. VJ Koller et al. describes the inhibition of cell division and the induction of a significant number of micronucleus that reflects structural or numerical chromosomal aberrations, so the use of these cannabinoids may produce adverse effects on health, damaging genetic material (6)

Conclusions

The European Early Warning System (EWS) informs specially an increase in the detection of new cannabinoids that are sold like "legal alternatives" of marijuana. APINACA is currently not under international control and, as we can see in this review, there is a lack of evidence and it has been described a potential harm. Further characterization of pharmacodynamics and pharmacokinetics of the compound is needed and also it's necessary to know the actual epidemiology of the use of this substance in order to determine the impact of its consumption and provide more information in understanding the cannabinoid system.

References

(1) Uchiyama N, Kawamura M, Kikura-Hanajiri R, Goda Y (2012). Identification of two new-type synthetic cannabinoids, N-(1-adamantyl)-1- pentyl-1H-indole-3-carboxamide (APICA) and N-(1-adamantyl)-1-pentyl-1H-indazole- 3-carboxamide (APINACA), and detection of five synthetic cannabinoids, AM-1220, AM-2233, AM-1241, CB-13 (CRA-13), and AM-1248, as designer drugs in illegal products. Forensic Toxicol 30(2): 114-125
(2) Gandhi AS1, Zhu M, Pang S, Wohlfarth A, Scheidweiler KB, Liu HF, Huestis MA. First characterization of AKB-48 metabolism, a novel synthetic cannabinoid, using human hepatocytes and high-resolution mass spectrometry. AAPS J. 2013 Oct;15(4):1091-8. doi: 10.1208/s12248-013-9516-0. Epub 2013 Aug 3.
(3) 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 SciInt 227(1-3): 21-32.
(4) Expert Committee on Drug Dependence.APINACA, critical review report, Agenda ítem 4.9.Geneva, 16-20 June 2014 WHO.
(5) Hermanns-Clausen M, Kneisel S, Szabo B, Auwarter V (2013). Acute toxicity due to the confirmed consumption of synthetic cannabinoids: clinical and laboratory findings. Addiction 108(3): 534-544.
(6) Koller VJ, Ferk F, Al-Serori H, Mišík M, Nersesyan A, Auwärter V, Grummt T, Knasmüller S. Genotoxic properties of representatives of alkylindazoles and aminoalkyl-indoles which are consumed as synthetic cannabinoids. FoodChemToxicol. 2015 Mar 16;80:130-136. doi: 10.1016/j.fct.2015.03.004.

Acknowledgements: L. Galindo received a scholarship Rio Hortega (CM14 / 00111) Carlos III Institute of Health: Supported in part by a grant from Instituto de Salud Carlos III (ISCIII-FIS-FEDER-PI14/00715 and Red de Trastornos Adictivos RTA- RD12/0028/0009)

Red de Trastornos Adictivos · Universitat Autònoma de Barcelona · IMIM Institut Hospital del Mar d'Investigacions Mèdiques · INAD Institut de Neuropsiquiatria i Addiccions · Parc de Salut MAR Barcelona