

SYNTHETIC CANNABINOIDS AND THE SEROTONIN SYNDROME: AN UNFORESEEN ASSOCIATION

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Educational Objectives: Use of synthetic cannabinoids (SCs) has been increasingly associated with severe adverse effects, including deaths. SC intoxication is very different to cannabis one and shows common features with the serotonin syndrome.

Purpose Synthetic cannabinoid compounds belong to a new psychoactive class of substances misused as an alternative to marijuana (MJ). These compounds have been developed for research purposes and have never been tested in clinical human studies. Currently, SCs can be easily bought on a global level, both online and in local stores. We aimed here at identifying SC pharmacodynamics, effects/symptoms of intoxication and neurobehavioral sequelae in humans, with a focus on findings compatible/common to the serotonin syndrome.

Methods: A search was carried out on PubMed/Medline for the terms “synthetic cannabimimetics”, “synthetic cannabinoids”, “synthetic cannabis” in order to identify effects/symptoms of intoxication, neurobehavioral sequelae related to SC intake in humans.

Results: SC compounds are structurally dissimilar and incorporate indole moieties, not present in MJ. SC are full agonists on cannabinoid receptors (CB-rs) while cannabis main psychoactive, tetrahydrocannabinol (THC), exerts partial agonism on cannabinoid receptors. SCs visual hallucinations are described as fractals/trails/ashes of colour/geometric patterns [1]. Signs of intoxication are elevated heart rate; hallucinations; mydriasis; agitation; vomiting; and seizures; these signs are common in the serotonin syndrome. Indole is structurally similar to serotonin (5-HT), has activity on 5-HT receptors and is typically identified within indoleamine hallucinogens such as DMT. While 5-HT_{2A} receptors are the primary site of action for DMT (typically producing visual geometric hallucinations in the users), the agonism of 5-HT_{2A} receptors contributes substantially to the development of the serotonin syndrome.

Conclusions: Beside the well-known cannabimimetic properties, SC drugs could have additive hallucinogenic effects due to the indole moieties incorporated in their structures. SCs intake/intoxication can produce acute signs/symptoms/clinical findings belonging to the serotonin syndrome.

Literature Reference

[1] Spaderna, M., Addy, P.H., D’Souza, D.C., 2013. Spicing things up: Synthetic cannabinoids. *Psychopharmacology (Berl)* 228(4): 525–540.