Semi-synthetic cannabinoids: A potent concern

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Emily Warrender June 9, 2025

Semi-synthetic cannabinoids have recently emerged as ‘lighter’ or ‘legal’ alternatives to cannabis, but they may be equally potent and equally risky, younger cousins

The sale of semi-synthetic cannabinoids (SSCs) began in the US in 2019, where they were marketed as ‘legal’ alternatives to cannabis. Since then, 18 different SSCs have been reported across North and South America, as well as the EU[1], where they arrived in 2022 and quickly spread[2]. SSCs include popular compounds like Δ8-THC and HHC, commonly sold in vapes and edibles. These products have drawn significant attention in various media forums[3–5], but what exactly are SSCs? Why should we pay attention to SSCs? And how should we deal with SSCs?

What are semi-synthetic cannabinoids?

In 2018, the US Agricultural Improvement Act (the ‘Farm Bill’) loosened restrictions on the cultivation of industrial hemp[6]. This resulted in an explosion in hemp production and, subsequently, an oversupply of the hemp-derived extract CBD[7].

To avoid financial losses, many producers exploited a loophole in the Farm Bill that allowed them to derive novel psychoactive products from this surplus CBD[6], such as Δ^8-THC and HHC. These compounds are referred to as ‘semi-synthetic’ because they are synthesised using plant-based precursors, with many of them already present in cannabis in imperceptible quantities. This makes them distinct from fully synthetic cannabinoids like Spice or K2, which do not rely on plant-derived precursors for their synthesis.

Why should we pay attention to semi-synthetic cannabinoids?

Semi-synthetic cannabinoids are readily available and widely used As of October 2024, SSCs had been reported in 34 countries[1], with nationwide data from the US in 2023 showing that 12% of adults had used Δ^8-THC in the past year[8]. By December 2023, these substances had also been substances have also been reported in 23 of the 27 EU Member States, with HHC being the most widely detected [9]. Accurate data on SSC usage in the EU remains unavailable. However, their widespread use across Europe can be inferred by two factors, which have been shown to drive interest and use of SSCs[8,10–14] :

1. A largely unregulated commercial marketplace (before 2024).
2. The illicit status of cannabis in many countries.

Health risks associated with semi-synthetic cannabinoids

Between 2021 and 2022, 4,925 cases of Δ8-THC poisoning were reported to US poison centres, with 16% of these requiring hospitalisation[15]. Most exposures occurred in children and adolescents (54%), with those under six years old accounting for 58% of critical care unit admissions and 33% of major medical outcomes. Most of these exposures were due to accidental ingestion (99%). Poisonings were also eight times higher in states without Δ^8-THC regulations.

Thirty-seven HHC poisonings were also reported in France between January 2022 and May 2023[16], with 24 of these requiring medical treatment. Neurological (e.g., dizziness) and cardiovascular symptoms (e.g., sinus tachycardia) were common, which have also been seen in other poisonings involving HHC analogues[17,18].

Mental health difficulties also appear to arise in the context of SSC usage. An analysis of the Reddit forum r/Delta8 revealed that psychiatric symptoms – especially anxiety and paranoia – were the most common adverse events related to Δ^8-THC use.[19] The psychopathological effects of SSCs are supported by numerous case reports implicating them in the onset of psychosis[20–25]. New data from Ireland further endorses the potential for SSCs to induce psychosis, as 34% of patients admitted to University Hospital Galway between May 2023 and December 2024 with a first episode of psychosis were using HHC prior to admission[26].

The psychosis-inducing potential of SSCs is of particular concern, given their widespread use among adolescents[10,11]. Adolescent cannabis use has been consistently demonstrated to increase the risk of developing a psychotic disorder[27] and, given that SSCs have been shown to be pharmacologically similar to cannabis[28–31], their use in adolescence might raise later psychosis risk and place a great burden on many countries' already stretched psychiatric services.

How should we deal with semi-synthetic cannabinoids?

The potential harms of SSCs underscore the need for government action. The US Hemp Advancement Act of 2022 prohibited concentrations of more than 0.3% Δ^8-THC in hemp-derived products[32]. As of March 2024, 18 EU Member States had listed HHC as a controlled drug[9]. However, other nations have been very slow in responding to the proliferation of SSCs. As of May 2025, a commercial SSC market continues in Ireland.

Although the actions taken to date have generally demonstrated government willingness to address the threat posed by SSCs, controlling individual compounds is simply not enough to curb their use. SSC producers have a strong track record of innovation, bringing at least 18 different compounds to market since their initial detection in 2019[1]. Therefore, banning one SSC will simply lead to the creation of another. A phenomenon observed with the 'legal highs' of the 2000s.

Legislation like the Psychoactive Substances Act in Ireland(33) and the UK [34] were brought in to tackle challenges of this very nature, as they provide a blanket ban on all new psychoactive substances (NPSs). These Acts could be leaned upon again to

address the legal loopholes that producers would otherwise jump through to continue supplying SSCs.

Although these acts have successfully addressed many of the issues posed by NPSs[35], they have been strongly criticised by some, primarily due to evidence suggesting that they increase NPS-related harm[36,37]. Innovative legislation like Czechia's psychomodulatory substance regulations, attempt to address the legal grey area occupied by SSCs by establishing a new classification system that promotes harm reduction and addresses the commercial aspects of drug control[38]. This might allow for more nuanced, evidence-based policy decisions, however, these regulations are yet to be implemented.

The time to act is now

There might be no perfect solution to the problems posed by SSCs, but given their substantial health risks, they must be regulated. Whatever the course of action chosen, governments that have not already acted must do so now!

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