

# Analysis of synthetic cannabinoids in abstinence control: long drug detection windows in serum and implications for practitioners

## Dear Editor,

The consumption of herbal mixtures containing synthetic cannabinoids, frequently used as a 'legal' alternative to cannabis,<sup>[1]</sup> has become an increasing issue of concern within emergency rooms<sup>[2,3]</sup> and therapeutic facilities.<sup>[4,5]</sup> In order to confirm the consumption of synthetic cannabinoids, blood analysis using highly specific and sensitive analytical methods, such as liquid chromatography-tandem mass spectrometry (LC-MS/MS), is essential.<sup>[6–9]</sup> Abstinence control subsequent to confirmed drug use requires the implementation of follow-up analyses, and in such cases, the interpretation of laboratory results is of particular importance, as drugs may accumulate in the body after chronic exposure, leading to prolonged windows of detection.<sup>[10]</sup>

Controlled studies on the elimination kinetics and the long-term detection of synthetic cannabinoids in humans are lacking and will most probably not become available in the near future because of the unfavorable risk profiles of these substances. For this reason, we aim to share our observations on this topic after having analyzed more than 4200 serum samples for synthetic cannabinoids until late 2012. The samples were received from patients of forensic psychiatric clinics, rehabilitation clinics or withdrawal treatment centers located in two different regions of Germany (federal states of Baden-Württemberg and Bavaria as well as Lower Saxony). Due to a high prevalence of synthetic cannabinoid use, most of the institutions sent follow-up samples from patients who tested positive by LC-MS/MS analysis.

A particularly striking observation was made in a number of cases in which the widely used synthetic cannabinoids JWH-081, JWH-122 or JWH-210 were detectable for up to 102 days following self-reported cessation of drug use, leading to estimated terminal elimination half-lives of up to 41 days. Consistent with the claim of abstinence during this period, a continuous decrease of serum concentration levels was noted. This observation raised the possibility that synthetic cannabinoids may be extensively distributed into deeper compartments (e.g. fat tissue), hence leading to an extended window of detection due to redistribution of these substances into the bloodstream, especially following heavy consumption. Moreover, our preliminary data suggest that this effect is even more pronounced than in the case of  $\Delta^9$ -tetrahydrocannabinol, for which terminal elimination half-lives of up to 13 days were reported.<sup>[10]</sup> As the concentration levels in the late stages of elimination are low and are seen to decrease slowly, it might have to be considered that they may also vary depending on the extent of lipometabolism influenced by diet, stress or certain medications such as hormones, anti-

diabetics, statins, and others. As a consequence, this may even lead to slightly increasing serum concentrations in consecutive serum samples.

In summary, these findings strongly suggest that synthetic cannabinoids are detectable in serum up to several months after cessation of drug use depending on the extent and duration of consumption. After confirmed use of synthetic cannabinoids, it seems advisable to consider the analysis of follow-up samples to be carried out at regular intervals (e.g. weekly), since, for the correct interpretation of analytical results, it is essential to monitor the concentration course. A conclusion drawn from these observations is that as long as additional synthetic cannabinoids or significantly higher substance concentrations cannot be detected in a positive follow-up sample, low serum concentration values have to be regarded as a consequence of long terminal elimination half-lives. Therefore, in cases of doubt a renewed consumption should not be automatically implied from just positive confirmation alone. The extent to which these observations may apply to the increasing number of newly identified synthetic cannabinoids remain to be investigated in the future but the implications of potentially long detection windows seem far-reaching.

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