## K63 Cannabinoid Receptor Bioassay: A Characterization of UR-144, XLR-11, and Their Metabolites and Degradants

*Kelsey Longe, BS*, Marshall University Forensic Science Program, 1401 Forensic Science Drive, Huntington, WV 25701; Amy B. Cadwallader, PhD, Aegis Sciences Corporation, 365 Great Circle Road, Nashville, TN 37228; Darcie Wallace-Duckworth, PhD, 515 Great Circle Road, Nashville, TN 37228-1310; and Pamela J. Staton, PhD, Marshall University Forensic Science MSFS & Center, 1401 Forensic Science Drive, Huntington, WV 25701*

After attending this presentation, attendees will better understand the cannabimimetic nature of UR-144, XLR-11, and their associated metabolites and degradants.

This presentation will impact the forensic science community by providing supporting evidence for the continued scheduling of UR-144, XLR-11, and some of their associated degradants and metabolites.

Synthetic cannabinoids, one of the largest-growing and widely varying groups of designer drugs, have become popular in recent years due to the cannabimimetic high they offer to users.[1] The similarities in the effects of synthetic cannabinoids and marijuana ($\Delta^9$-tetrahydrocannabinol) are thought to be the result of these compounds interacting with the same G Protein-Coupled Receptors (GPCRs).[2] These GPCRs are more commonly referred to as the cannabinoid binding receptors CB1 and CB2 and are located in the body's central and peripheral nervous systems, respectively. Due to their separate locations, CB1 receptors are generally associated with the hallucinogenic effects of cannabinoids, while the CB2 receptors are linked to the therapeutic effects of cannabinoids; however, very little has been discovered regarding the potencies of these compounds at these receptors.[3] This lack of information regarding the cannabimimetic nature of these drugs makes it difficult for authorities to schedule them.

In order to learn more about how different synthetic cannabinoids interact with the CB1 and CB2 receptors, the potency ($EC_{50}$) of two of these synthetic cannabinoids, UR-144 and XLR-11, as well as ten of their metabolites and degradants, was investigated using a mammalian cell-based cannabinoid receptor bioassay. For UR-144, $EC_{50}$ values of 8.5ng/mL and 3.6ng/mL were found for the CB1 and CB2 receptors, respectively. Two of the remaining UR-144 compounds, the UR-144 degradant and the N-(2-hydroxypentyl) metabolite, were determined to be more potent at the CB1 receptors, while the N-(4-hydroxypentyl) and N-(5-hydroxypentyl) metabolites both were found to be more potent than UR-144 at the CB2 receptors. With XLR-11, the CB1 and CB2 $EC_{50}$ values were found to be 101ng/mL and 6.6ng/mL, respectively. All three XLR-11 metabolites and degradants tested proved to be more potent than XLR-11 at the CB2 receptors, with one of these three compounds being more potent at the CB1 receptors as well. Combining the knowledge that seven of the ten metabolized and degraded forms of UR-144 and XLR-11 tested demonstrated greater potencies than the parent compounds, and the fact that the metabolized and degraded forms are likely to be more commonly seen in forensic toxicological samples than UR-144 and XLR-11 themselves, it can be suggested that the bioassay shows great potential as a screening method for toxicological samples.

In conclusion, this study's results support the claim that several of the UR-144 and XLR-11 compounds are cannabimimetic due to their activity with the CB1 and CB2 receptors. This data is not only applicable to forensics by helping determine if these drugs should continue to be scheduled, but it can also be useful to the field of medicinal chemistry in which cannabinoids with a greater potency at the CB2 receptors than the CB1 receptors are being investigated as potential therapeutic treatments.[4]

**Reference(s):**

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**UR-144, XLR-11, Cannabinoid Binding Receptors**





*Presenting Author