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# PHARMACOKINETICS AND PHARMACODYNAMICS OF THE SYNTHETIC CANNABINOID UR-144 AND ITS HALOGENATED ANALOGUE 5F-UR-144 (XLR-11)

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The new drug of abuse UR-144 [1-pentyl-1H-indol-3-yl)-(2,2,3,3-tetramethylcyclopropyl)methanone] and its halogenated form XLR-11 [5F-UR-144 or (1- (5-fluoropentyl)-1H-indol-3-yl)-(2,2,3,3-tetramethylcyclopropyl)methanone] are potent alkylindole synthetic cannabinoids that have been recently identified in herbal mixtures with tobacco, incense and potpourri. Most data available on UR-144 and XLR-11 come from clinical and forensic reports of intoxications.

## **INTOXICATION EFFECTS**

Intoxication symptoms include an increase in the muscular tonus, high systolic arterial pressure, anxiety, incoherent speech, impaired coordination, hallucinations, irritability, seizures, tachycardia and chest pain. Acute kidney injury (acute tubular injury and interstitial nephritis), pulmonary oedema, brain stroke and myocardial ischemia are frequently described in autopsies

#### TOXICOKINETICS

UR-144 and XLR-11 are mainly metabolized at the hepatic level,



especially by CYP3A4. CYP1A2 also appears to contribute, at a minor scale, to compound metabolism. For XLR-11, the substitution of the fluorine atom by an hydroxyl group seems to be an important metabolic reaction, but several other metabolites co-occur for both drugs. Products of monohydroxylation, dihydroxylation and/or formation of the N-pentanoic acid were among the most abundant metabolites detected in human urine.



Figure 3. Metabolic pathway of XLR-11



Figure 1. Comparison of the physiological effects of Cannabis ('Marijuana') and the synthetic cannabinoids XLR-11 and UR-144

## PHARMACOLOGY

XLR-11 and UR-144 display low, nanomolar affinity for the cannabinoid receptors 1 and 2 (CB1 and CB2, respectively), and are capable of binding to both, more strongly than  $\Delta$ 9–tetrahydrocannabinol (THC). UR-144 has great affinity for the CB2 but substantial lower affinity for the CB1, while XLR-11 shows a potent agonist effect in both cannabinoid receptors.



Figure 4. Metabolic pathway of UR-144

#### HIGHLIGHTS

- A considerable number of hospitalizations following UR-144 and XLR-11 acute exposure resulted in severe or fatal outcome
- The mechanisms underlying their toxicity are not yet thoroughly documented
- It is presently unknown to which extent metabolic reactions contribute to the (de)toxication of the drugs
- The information is also scarce regarding the long-term toxicity
- Further clinical and forensic toxicological studies are urgently required

**Conflict of Interest:** The authors declare that they have no conflict of interest

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#### **Figure 2**. Pharmacodynamic profile of XLR-11 and UR-144



