# Structure Activity Relationship of Drugs of Abuse

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## AIMS

**The study aimed at identifying links between structural modifications and physiological effects , adverse effects and toxicities of synthetic cannabinoids, cathinones and opioids.**

## METHODS

**Literature review identified the functional groups of the external structural backbone of synthetic drugs of abuse in relation to adverse drug reactions, toxicities and physiological effects of amino alkyl indoles, synthetic cathinones and fentanyl analogues.**

## RESULTS

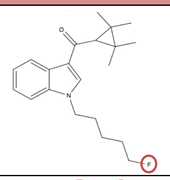
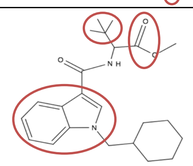
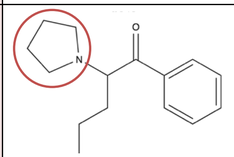
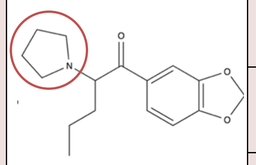
| | Molecular Structure | Adverse Drug Reaction (ADR) | Cause of ADR |
|---|---|---|---|
| **XLR-11** (Synthetic Cannabinoid) |  | Acute Kidney Injury | Overstimulation of $CB_1$ receptors in kidney cells caused by the high potency and selectivity of XLR-11 and its pyrolysis products to $CB_1$ receptors |
| **MDMB-CHMICA** (Synthetic Cannabinoid) |  | Acute Kidney Injury | Overstimulation of $CB_1$ receptors in kidney cells caused by high selectivity of MDMB-CHMICA to CB1 receptors due to presence of indole core, tert-leucine group and ester link. |
| **A-PVP** (Synthetic Cathinone) |  | Psychosis and Delirium | Potent inhibitory uptake effects at dopamine transporter and norepinephrine transporter due to presence of pyrrolidine ring. |
| **MDPV** (Synthetic Cathinone) |  | Psychosis and Delirium | Potent inhibitory uptake effects at dopamine transporter and norepinephrine transporter due to presence of pyrrolidine ring. |
| | | Rhabdomyolysis | Increased muscular activity caused by sympathomimetic stimulation and hyperthermia. |
| | | Disseminated Intravascular Coagulation | Dopamine induced hyperthermia |

**Table 1: Table showing drug of abuse, molecular structure, adverse drug reaction and cause for ADR for XLR-11, MDMB-CHMICA, α-PVP and MDPV.**

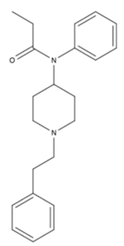
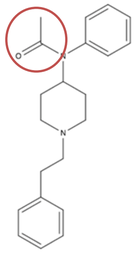
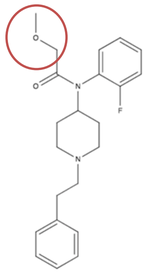
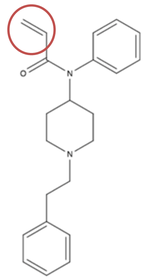
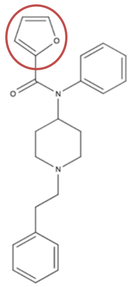
| Drug of abuse | Fentanyl | Acetylfentanyl | Ocfentanil | acryloyfentanyl | Furanylfentanyl |
|---|---|---|---|---|---|
| **Molecular Structure** |  |  |  |  |  |
| **Lipophilic Character** | XLogP=4.0 | Lower Lipophilic character than fentanyl (XLogP=3.6) | Lower Lipophilic character than fentanyl (XLogP=3.6) | Higher Lipophilic character than fentanyl (XLogP=4.2) | Higher Lipophilic character than fentanyl (XLogP=4.6) |
| **Duration of Physiological effects** | 30-60 minutes | Lower duration of effects when compared to fentanyl | Lower duration of effects when compared to fentanyl | Higher duration of effects when compared to fentanyl | Highest duration of effects when compared to fentanyl |

**Table 2: Table showing link between drug of abuse, molecular structure, lipophilic character and duration of physiological effects of fentanyl analogues.**

## CONCLUSION

**The physiochemical changes brought about by structural modifications to produce synthetic drugs of abuse are linked to changes in potencies and changes in types and duration of effects.**

**Synthetic cannabinoids and synthetic cathinones are linked to increased adverse effects and toxicities. Fentanyl analogues displayed similar effects and toxicities to those of earlier developed opioids but differed in duration of effects.**

**This study contributes to an explanation of the higher potencies, toxicities and adverse drug reactions associated with the abuse of synthetic drugs.**