Drug abuse of novel psychoactive substances (NPS) is becoming increasingly popular among young people, particularly within the Electronic Dance Music (EDM) scene. Often, newly popular drugs on the market may be minor modifications of more well-known drugs, allowing them to be developed, marketed, and distributed online while circumventing the law. These designer drugs are rapidly introduced to the market and are quickly modified, and the metabolic pathway of many of these remains largely unknown. This information is essential for detecting prior usage of drugs. Although there is research concerning the metabolism of certain NPS drugs, it remains a constantly changing market, and new drugs with unstudied metabolic pathways continue to be introduced and popularized as recreational drugs. The intent for this study was to use human liver microsomes to generate metabolites of two NPS compounds (α-PVP and dimethylone, shown in figures 1 and 2) and identify these metabolites by analysis with Ultra Performance Liquid Chromatography/Quadrupole Time of Flight Mass Spectrometry (UPLC/Q-TOF).

**Methods**

The method for in vitro metabolism by human liver microsomes was first optimized by incubation with diazepam. The variables optimized were the amount of drug, NADPH, and magnesium chloride. The optimized method for in vitro metabolism was successfully used to metabolize α-PVP and dimethylone into metabolites, which were identified by UPLC/Q-TOF. The metabolic pathways of α-PVP were hydroxylation, reduction of the ketone to an alcohol, degradation of the pyrrolidine ring to an amine, and oxidation of the pyrrolidine ring to a lactam followed by ring opening and reduction to the corresponding alcohol. The observed metabolic pathways of dimethylone were demethylation followed by methylolation, and dealkylation into methylone. However, the metabolic products observed in the dimethylone incubation (dealkylation, demethylation, and hydroxylation of methylone) were not seen as products of dimethylone metabolism. The metabolic profile of dimethylone has not been previously reported, and future work includes confirming these metabolites by analysis of authentic urine samples of users.

**Discussion**

The optimized method for in vitro metabolism was successfully used to metabolize α-PVP and dimethylone into metabolites, which were identified by UPLC/Q-TOF. The metabolic pathways of α-PVP were hydroxylation, reduction of the ketone to an alcohol, degradation of the pyrrolidine ring to an amine, and oxidation of the pyrrolidine ring to a lactam followed by ring opening and reduction to the corresponding alcohol. The observed metabolic pathways of dimethylone were demethylation followed by methylolation, and dealkylation into methylone. However, the metabolic products observed in the dimethylone incubation (dealkylation, demethylation, and hydroxylation of methylone) were not seen as products of dimethylone metabolism. The metabolic profile of dimethylone has not been previously reported, and future work includes confirming these metabolites by analysis of authentic urine samples of users.

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