K60 Physiochemical Characterization of 19 Fentalogs: Lipophilicity

Madison R. Schackmuth, BS, Huntsville, TX 77320; Sarah Kerrigan, PhD, Sam Houston State University, Department of Forensic Science, Huntsville, TX 77341*

Learning Overview: After attending this presentation, attendees will have increased understanding regarding the physicochemical properties of fentanyl analogs (fentalogs) and their importance in forensic science.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by providing additional information concerning the lipophilicity of fentalogs and their overall impact in terms of analytical separations and the interpretation of results.

Forensic toxicologists are tasked with the identification of New Psychoactive Substances (NPS) in biological matrices and may be required to interpret their findings. Yet, the physiochemical properties of these new and emerging drugs are not always known. Although fentanyl and a small number of derivatives used for medical or veterinary procedures are well characterized, physiochemical properties have not been determined for many emerging fentanyl analogs. Lipophilicity plays an important role in terms of separation and analytical determination, as well as the overall pharmacology of the drug (i.e., absorption, distribution, metabolism, and excretion). It is described by parameters such as partition coefficients (log P/log D) and Volume of distribution (V_d).

Partition coefficients were determined for 19 fentalogs. Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) was used to experimentally determine partition coefficients (octanol/water) for (+)-cis-3-methylfentanyl, 4-ANPP, acetylfentanyl, butyrylfentanyl, isobutyrylfentanyl, furanylfentanyl, valerylfentanyl, norfentanyl, norcarfentanil, alfentanil, remifentanil, sufentanil, carfentanil, p-fluoroisobutyrylfentanyl, p-fluorobutyrylfentanyl, p-fluorofentanyl, o-fluorofentanyl, and β-hydroxythiofentanyl. An Agilent® 1290 Infinity LC coupled to an Agilent® 6470 triple quadrupole mass spectrometer was employed in positive Electrospray Ionization (ESI) mode. Fentalogs were separated using gradient elution using a mobile phase consisting of deionized water/acetonitrile containing 0.1% formic acid. Data were acquired using Multiple Reaction Monitoring (MRM) and data analysis was performed using Agilent® MassHunter™ software. Source conditions were optimized for all analytes and chromatographic resolution was achieved for all 19 fentalogs.

Experimentally determined partition coefficients were compared with specialized software-generated data from three independent sources (ACD, ALogPS, and LogKOW). Log D values for the 19 fentalogs were measured over a wide range (<0.1 to 2.7) in octanol/water. Partition coefficients were also evaluated over a range of pH values in aqueous buffer systems. The results highlight important differences in the lipophilicity of fentalogs with phenethyl, piperidine, aniline, or *N*-propionyl substitutions. Although numerically determined partition coefficients can be of value for forensic chemistry and toxicology applications, the comparison of experimental and software-generated data can provide important insight regarding future fentalogs that have yet to emerge. Per research, this study may be the largest characterization of fentalog lipophilicity to date. The observed differences in lipophilicity can have important implications in terms of the pharmacology and toxicology of these synthetic opioids.

Fentalogs, Partition Coefficients, Log P/log D