EXPERIMENTAL DETERMINATION OF CHEMICAL SOLUBILITY IN WATER

The Chemical Security Analysis Center's (CSAC) Chemical Security Lab (CSL) at the Department of Homeland Security (DHS) Science and Technology Directorate (S&T) is measuring chemical and physical properties for compounds that are in the S&T Risk Assessments. The solubility of chemicals affects the dose that is delivered in the various attack scenarios in the risk assessments, and therefore accurate solubility values are important for the calculation of human health consequences.

The CSL has utilized two orthogonal published methods[1] for the determination of chemical solubility in water and will expand this methodology to additional matrices.

MATERIALS

Chemicals: caffeine, 4-aminopyridine, aniline, carbofuran, vanadium pentoxide, and 1-phenylsilatrane were obtained from Sigma-Aldrich. Analysis was performed using a ThermoFisher Nanodrop 2000 Ultraviolet-visible (UV-Vis) spectrophotometer and a BMG LabTech NEPHELOstar Nephelometer.

METHODOLOGY

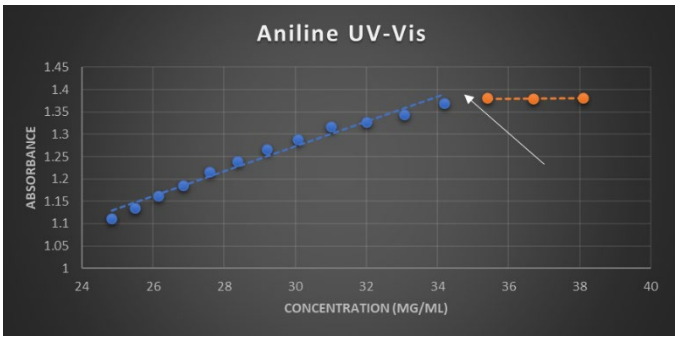
UV-Vis Spectroscopy

Each chemical was dissolved in a solution of 100% dimethyl sulfoxide (DMSO) and 5% DMSO with distilled water as the transport medium (TM) for these experiments. Further dilutions (minimum of 7) of each solution were prepared and analyzed on the Nanodrop UV-Vis spectrophotometer. A plot was made using these points to determine if solubility had been achieved (e.g., **Figure 1**), and then the same concentrations in each matrix were analyzed and solubility was determined as in **Equation 1**:

$$solubility\ (\mu M) = \frac{Abs\ of\ compound\ in\ TM\ containing\ 5\%\ DMSO}{Abs\ of\ compound\ at\ Conc\ (\mu M)\ in\ 100\%\ DMSO}\ x\ Conc\ (\mu M)$$

Equation 1. Calculation Used to Determine Solubility for UV-Vis[1] Data

Figure 1. Solubility Curve of Aniline Using the UV-Vis Spectrophotometer

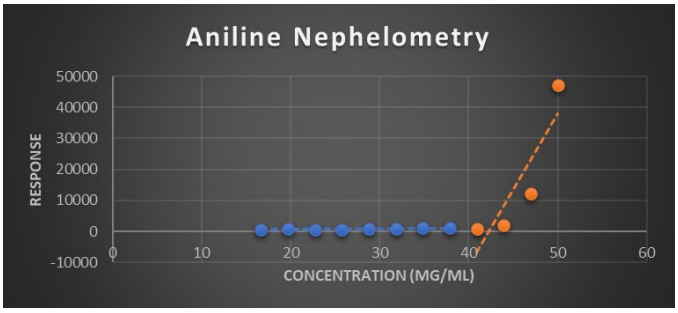


NOTE: The orange dots are above the solubility and the blue line is the linear indication that aniline has dissolved fully. The arrow indicates the point where the slope changes dramatically, which is indicative of the solubility point. This is the concentration that was used for part two of the UV-Vis method.

Nephelometry

Twelve concentrations of the chemical dissolved in 5% DMSO in TM (distilled water) were run on the nephelometer. A concentration curve was made, and the solubility point was determined by the intersection of the lines based on the sudden change in slope (e.g., **Figure 2**).

Figure 2. Solubility Curve of Aniline Using the Nephelometer



NOTE: The orange dots are above the solubility and the blue line is the linear indication that aniline has dissolved fully. The arrow indicates the solubility point. This point was determined by calculating the intersection of the two lines based on the linear equations.

RESULTS

Table 1. Experimental and Current S&T Risk Solubility Values

Chemical	Nephelometer Solubility (mg/mL)	UV-Vis Solubility (mg/mL)	Solubility Used in S&T Risk (mg/mL)
Caffeine	20.12	11.75	21[2]
4-Aminopyridine	72.17	85.5	72[2]
Aniline	42.52	34.4	35[2]
Carbofuran	0.22	0.17	0.35[3]
Vanadium Pentoxide	0.91	N/A[a]	0.9[4]
1-Phenylsilatrane	0.078	0.087	228[2]

NOTE: [a]N/A=not applicable. Due to the orange coloring UV-Vis is not a viable method.

DISCUSSION

The solubility points determined by the orthogonal methods differed by varying amounts, resulting in a solubility range for each compound. The experimentally determined solubility values will be used to update data in the S&T Risk models. The experimental data enabled clearly erroneous data to be identified and corrected, which is critical for risk modeling to be trusted and utilized. Comparing these methods and the results provides a more concise view of solubility. The lab is working to complete the matrix by finalizing the UV-Vis methods for carbofuran and vanadium pentoxide. Additional compounds are being considered for this work as well as the expansion to new matrices like hand sanitizer.

REFERENCES

1. Pan, L.; Ho, Q.; Tsutsui, K.; Takahashi, L. Comparison of chromatographic and spectroscopic methods used to rank compounds for aqueous solubility. *J. Pharm. Sci.*, **2001,** *90* (4), 521–529.
2. Brevett, C.A.S; Bradley, D.R.; Morton, D.W.; Pennington, T.E. *Chemical Characteristics for Anticoagulant, Blood, Convulsant, Encephalopathy, Hemolytic/Methemoglobinemia, Metabolic, Opioid, Sympathomimetic/Stimulant, and Vesicant Agents of Concern*; CSAC 23-015; U.S. Department of Homeland Security, Science and Technology Directorate, Chemical Security Analysis Center: Aberdeen Proving Ground, MD, 2023. (U//FOUO)
3. Brevett, C.A.S; Bradley, D.R.; Morton, D.W.; Pennington, T.E. *Chemical Characteristics for Cholinergic Agents of Concern*; CSAC 23-011; U.S. Department of Homeland Security, Science and Technology Directorate, Chemical Security Analysis Center: Aberdeen Proving Ground, MD, 2023. (U//FOUO)
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