Synthesis and Analysis of Hydrochloride Salts Used as Adulterants

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Abstract

An adulterant is an additive commonly found in the illicit drug trade. These adulterants are used to bulk up the drug supply and increase the potency of the drug. Adulterants can be many compounds, from chemicals to poisons. Sugars, prescription medications, metals, and even pesticides can be used for this purpose (1). An over-the-counter drug can also be used as an adulterant. A common practice is to dissolve this drug in hydrochloric acid and allow it to recrystallize. The recrystallized version becomes a hydrochloride salt form of the adulterant. This new form has an increased molecule size and water solubility. Increasing the water solubility will increase the drug's ability to enter the body system and decrease the amount of time required to experience the effect of the drug. In this study, four over-the-counter drugs were chosen for experiment and analysis: caffeine, ibuprofen, quinine, and acetaminophen. These were each dissolved in different volumes of 1M hydrochloric acid and were allowed time to recrystallize. The crystals were then analyzed using various methods such as IR, SEM-FE/EDX, melting point, and water solubility.

Introduction

The common adulterants examined in this experiment are added to a variety of street drugs. Caffeine is added to cocaine, heroin, methamphetamine, ecstasy, and amphetamine due to its properties as a psychoactive stimulant (2). Caffeine has milder yet similar effects as cocaine, methamphetamine, ecstasy, and amphetamine (2). When caffeine is added to heroine, the mixture's vaporization temperature decreases allowing the street drug to enter the body at a higher rate (2). Quinine is added to heroin due to having a similar bitterness and effect when injected (2). Ibuprofen is added to cocaine and is thought to cause lung damage when inhaled with cocaine (3). The last adulterant, acetaminophen, is used with cocaine and heroin due to affecting the individual in a similar way as a cutting agent (4). A cutting agent is a substance that reduces the purity of the street drug in question (4).

Methods

12 M concentrated hydrochloric acid was diluted to 1M with de-ionized water. About 0.25g of ground (in a mortar and pestle) over-the-counter drugs including ibuprofen, acetaminophen, and caffeine, were dissolved in both 10mL and 5mL of the 1M HCl (aq). The ibuprofen was not soluble in HCl (aq) and thus rejected from further experimentation. These were stored undisturbed for several weeks to allow recrystallization in the form of hydrochloride salts. Once recrystallized, all products including the drug before recrystallization in HCl (aq), were analyzed using infrared spectroscopy. Next, these crystals' water solubility were analyzed. For the caffeine crystals, 0.1g of the 10 mL, 5 mL, and unchanged drug were dissolved in 20 mL of tap water. For the acetaminophen crystals, 0.02g of the 10 mL, 5 mL, and unchanged drug were dissolved in 20 mL of tap water. Quinine was also analyzed in this way, dissolving 0.1g of the different crystals and the unchanged drug in 20 mL of water. The time it took to dissolve in water, or inability to dissolve in water, was recorded. In addition to this, 0.52g of caffeine was dissolved in 10 mL of 1M HCl (aq). This sample was stored undisturbed and checked every few weeks for crystal growth. Additionally, pill form acetaminophen was crushed into a powder using a mortar and pestle. Next, .501g of the powder was heated and dissolved in a total of 12.5 mL 1M HCl (aq). Two quinine samples were prepared by fully dissolving 44g and .50g of quinine each in 3.5mL of 1M HCl. To thoroughly analyze the samples, detailed imaging of the crystalline structure as well as compositional data was obtained as follows. Once there was significant crystal formation (indicating a hydrochloride salt) with no remaining aqueous sample (approximately 2-4 weeks after initial preparation) a portion of the caffeine and acetaminophen samples was gold-plated and analyzed using energy dispersive X-ray analysis (EDX) and/or field emission scanning electron microscopy (FE-SEM).

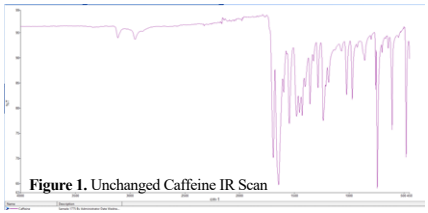

Figure 1. Unchanged Caffeine IR Scan

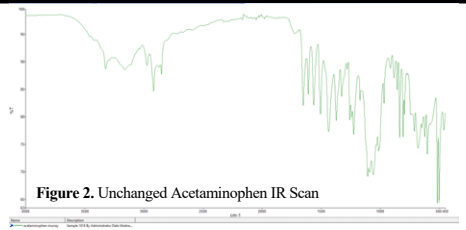

Figure 2. Unchanged Acetaminophen IR Scan

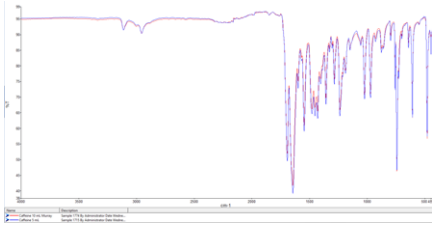

Figure 3. 10mL and 5mL Recrystallized Caffeine IR Scan Overlay

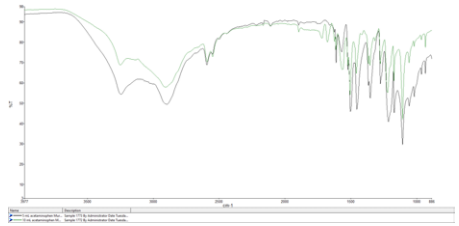

Figure 4. 10mL and 5mL Recrystallized Acetaminophen IR Scan Overlay

Figure 5. Recrystallized Caffeine in 5mL of HCl

Figure 6. Recrystallized Caffeine in 10mL of HCl

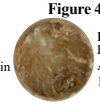

Figure 7. Recrystallized Acetaminophen in 5mL of HCl

Figure 8. Recrystallized Acetaminophen in 10mL of HCl

Figure 9. Recrystallized Quinine in 3.5mL of HCl

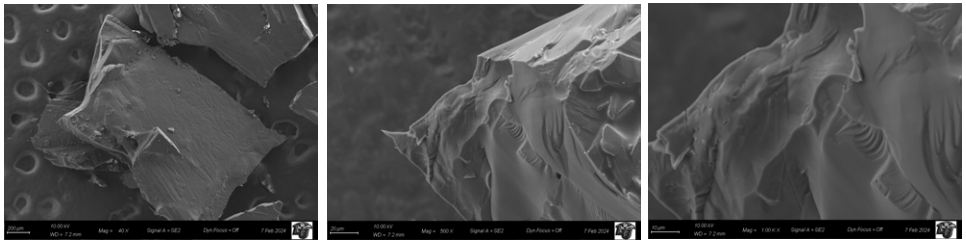

Figure 10. Surface structure of crystalline hydrochloride salt synthesized from acetaminophen viewed under a FE-SEM at increasing resolutions of 40x, 500x, and 1000x, respectively

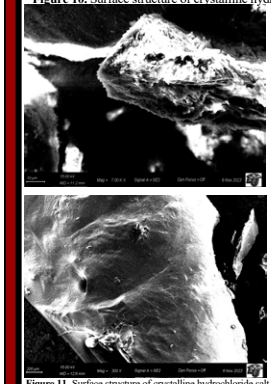

Figure 11. Surface structure of crystalline hydrochloride salt synthesized from caffeine viewed under a FE-SEM

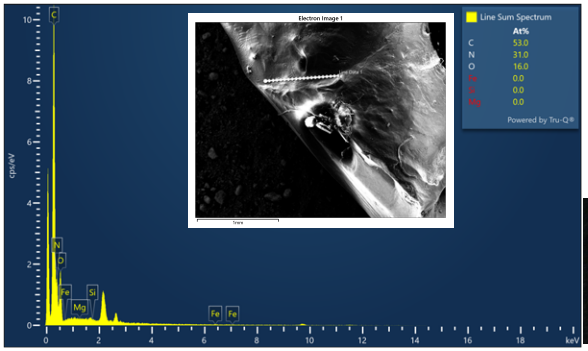

Figure 12. Graph from SEM-EDX of the caffeine hydrochloride salt providing insight into its chemical composition. Line data 1 indicates a composition of 53% carbon, 31% nitrogen, and 16% oxygen.

Figure 13. Hydrochloride salt recrystallized from .501g acetaminophen in 12.5 mL of HCl

Figure 14. Hydrochloride salt recrystallized from .52g caffeine in 10 mL of HCl

Results and Conclusion

After the recrystallization of the caffeine and ibuprofen in both 10mL and 5mL of 1M HCl (aq), the products as well as the unchanged drugs were analyzed using infrared spectroscopy. In comparing the unchanged caffeine to both versions of the recrystallized hydrochloride salt (see Figures 1 and 3), little to no change was observed. All scans show prominent peaks in the same areas (such as in the 1600 cm^{-1}, 1500 cm^{-1}, and 700 cm^{-1} regions). This points to the conclusion that the recrystallization of caffeine in HCl does not change its structural composition. This, however, was not the case for the acetaminophen (see Figures 2 and 4). In comparing the unchanged acetaminophen to both samples of the recrystallized hydrochloride salt forms, several differences can be seen. The most prominent change is in the sample that was dissolved in 5 mL of HCl. While the unchanged version has a shallow dip in peaks in the 2500 cm^{-1} to 3500 cm^{-1} region, the hydrochloride salt sample displays a much more dramatic, deeper peak in this region. The unchanged version also has a prominent peak in the 1100 cm^{-1} region while the 5 mL hydrochloride salt sample displays this to a much lesser degree, and the 10 mL hydrochloride salt sample hardly displays this at all. This points to the conclusion that the recrystallization of acetaminophen in HCl does change its structural composition.

The recrystallized caffeine, acetaminophen, and quinine were also analyzed by their water solubility. All samples were dissolved in tap water. The 10 mL recrystallized hydrochloride salt of caffeine took 16 minutes and 49 seconds to dissolve, the 5 mL sample took 17 minutes to dissolve, and the unchanged caffeine took 5 minutes and 43 seconds to dissolve. This points to the conclusion that recrystallizing caffeine in hydrochloride salt decreases its water solubility. The 10 mL recrystallized hydrochloride salt of acetaminophen took 3 minutes and 59 seconds to dissolve, the 5 mL sample took 2 minutes to dissolve, and the unchanged acetaminophen did not dissolve at all. This points to the conclusion that recrystallizing acetaminophen in hydrochloride salt greatly improves its water solubility. Finally, the 0.5g recrystallized hydrochloride salt of quinine took 1 minute and 10 seconds to dissolve, the 0.44g sample took 1 minute and 20 seconds to dissolve, while the unchanged quinine did not dissolve at all. This points to the conclusion that recrystallizing quinine in hydrochloride salt greatly improves its water solubility.

Overall, the degree of change of an over-the-counter drug to its hydrochloride salt version varies depending on the drug in question whether in the context of its chemical structure or solubility.

According to the energy dispersive X-ray analysis, the atomic percentage of the caffeine hydrochloride salt at line data 1 was 53% carbon, 31% nitrogen, and 16% oxygen. It is worth noting that any hydrogen atoms in the salt cannot be detected using SEM-EDX (5). Given this fact, the results from the SEM-EDX supports the conclusion that the recrystallization process did not significantly alter the hydrochloride salt from its original composition. Thus, the atomic percentage aligns with the composition one would expect of a caffeine derived substance.

Future Work

1. Testing of additional over-the-counter medications that could function as hydrochloride salts would be informative especially in the context of their various industry applications.
2. Comparative analysis of most effective ratio of mL hydrochloric acid to grams of given over-the-counter medication based on length of recrystallization and quality of product.
3. Testing the impact of various molar concentrations of HCl on the time for recrystallization and the quality of the resulting hydrochloride salt would aid in the development of more efficient recrystallization methods.

References and Acknowledgments

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Special thanks to Stephen Horstemeyer for training on the SEM, Kate Ferro and Abigail Kimmey for additional SEM assistance, and Angielisa Sirard for assistance with the infrared spectrometer.