FINAL SUMMARY OVERVIEW

Development of Modern Microcrystal Tests for Controlled Drugs, Diverted Pharmaceuticals and Bath Salts

Cooperative Agreement 2015-IJ-CX-K010
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1.0 Purpose

There are a number of controlled substances for which there are presently no known microcrystal tests. This research addresses the lack of simple, readily available testing methods for selected controlled substances by developing new microcrystal tests and providing the details of each test. Twelve (12) controlled substances (Table 1) were selected for which no microcrystal tests are currently available. These 12 drugs and the microcrystal test conditions resulting from this research will be included in the Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals (Microcrystal Compendium) originally developed and compiled by McCrone Research Institute and available as a free high-resolution PDF for viewing or download at www.mccroneinstitute.org or the Office of Justice Programs' NCJRS website.

The new microcrystal tests and procedures were vetted, developed, and reviewed by McCrone forensic research and senior research microscopists and instructors in voluntary collaboration with practicing forensic scientists in other laboratories. Each microcrystal test developed and selected for addition to the Microcrystal Compendium will include recommended protocols and morphologies of crystals including photomicrographs, infrared spectra of microcrystals, potential interferences, and optical crystallographic properties of the resultant microcrystals.

Table 1: List of Drugs Included in Project

Table 1. Drugs Included in This Project

Drug	Trade Name
Alprazolam	Xanax
Buprenorphine*	Buprenex, Subutex, Suboxone, Butrans
Butylone	Commonly found in "bath salts," (aka β-keto-N-methylbenzodioxolylbutanamine, bk-MBDB). Not a pharmaceutical.
Carisoprodol*	Soma
Lorazepam*	Ativan
Mephedrone	Commonly found in "bath salts." Not a pharmaceutical.
Mehtylenedioxypyrovalerone	Commonly found in "bath salts," (aka MDPV). Not a pharmaceutical.
4-Methylethcathinone	Commonly found in "bath salts," (aka 4-MEC). Not a pharmaceutical.
Methylone	Commonly found in "bath salts," (aka M1, MDMC). Not a pharmaceutical.
α-Pyrrolidinopentiophenone	Commonly found in "bath salts," (aka alpha-PVP). Not a pharmaceutical.
Tramadol	Ryzolt, Tramal, Ultram
Zolpidem	Ambien

*** Testing with these 3 drugs was ceased; no microcrystal tests discovered .**

The ideal microanalytical method for forensic drug analysis is an automated procedure performed by a technician covering all known drugs. This certainly applies to many analytical techniques used today including, for example, the combination of gas chromatography and mass spectroscopy (GC-MS). Light microscopy and microcrystal tests have been in use for more than 100 years but are not often regarded as a modern or ideal method; however, they are useful when the automated equipment is not available or when the analyst needs to check for the presence of one or more specific drugs. And while laboratories may lack some analytical capabilities, most laboratories

have microscopes and properly trained microscopists. If the analyst wishes to know whether a specific drug is present, the polarized light microscope (PLM) will answer this question very quickly and, compared to other methods, very inexpensively. In addition, certain methods of analysis for drug identification, for example those specified by SWGDRUG, require the use of multiple uncorrelated techniques. This indicates that a good use of microscopy and the PLM would be to check and confirm the results obtained by other methods. Inclusion of new microcrystal tests, including optical properties of resultant microcrystals to the modern Microcrystal Compendium, provides an excellent alternate technique and confirmatory method to give that added degree of confidence in the procedures and in the courtroom.

2.0 Project Design and Methods

Phase 1: Selection and evaluation of reagents

Various reagents were tested on the drug of interest (known standard) until suitable reagents and procedures were found. This trial-and-error approach of testing was not entirely random. Reagents were first determined as candidates based on their current availability, use, and success in microcrystal tests of related chemical compounds. The method therefore was developed from the technical literature, and known compounds of interest were subjected to rigorous testing. Once a reagent was found to form microcrystals, the reagent and test method were thoroughly evaluated. At least one reagent per drug (with the exception of buprenorphine, carisoprodol and lorazepam) and in some case two or more reagents, were selected based on the following attributes: time required before the formation of microcrystals; sensitivity of the

test; how well the test worked in the presence of common pharmaceutical formulations (for manufactured tablets or capsules), excipients, diluents, and adulterants (for the street drugs); comparison of resultant microcrystals with those formed using the same reagent on similar or related compounds; and final testing of the reagent on "real world" samples, e.g., pharmaceutical tablets.

Phase 2: Optics of microcrystals

This phase determined the optics of the microcrystals formed from the selected reagents and includes photomicrographs for illustration in the Microcrystal Compendium. Phase 2 is separate from the previous phase so that a second researcher could verify those test methods developed by the first researcher in Phase 1. This format was used in previous microcrystal research at McCrone and has been found to be an efficient and effective way of vetting test methods. Tests that formed microcrystals were first washed, to remove any reagent present. Then, the following optical properties of the microcrystals formed were determined: refractive index, color/pleochroism, birefringence, and sign of elongation. Infrared microspectroscopy was also performed on the microcrystals.

Phase 3: Peer review of protocols

Selected state, local, and university forensic science laboratories voluntarily collaborated with McCrone and assisted with assessing the methods, including the feasibility and suitability of the newly discovered microcrystal tests in the laboratory. This peer review of the protocols will ensure practicing forensic laboratories and university forensic science programs can use the methods, as well as integrate them easily into existing analysis schemes.

Phase 4: Compilation of the Microcrystal Compendium Data

This phase involved compiling all the data and results and preparation of the final individual monographs for addition to the electronic Microcrystal Compendium for dissemination to the forensic science community (see Appendix). The Microcrystal Compendium will be available as a free, high-resolution PDF for viewing or download on the www.mccroneinstitute.org website.

Phase 5: Final reports, preparation of scientific papers, and Microcrystal Compendium additions completed

This phase allowed for the composition and review of the draft summary report and the final summary report for submission to NIJ. The preparation of monographs for each drug and reagent to be submitted in scientific papers detailing the development of the new microcrystal tests to peer-reviewed journals, for example *the Journal of Forensic Sciences*, *The Microscope Journal*, *Microgram Journal*, *Forensic Science International*, etc., will also be completed during this phase.

3.0 Data Analysis and Project Findings

The current research discovered that 9 of the 12 drugs selected have two tests and reagents that produce microcrystals which were previously unknown. Three drugs, buprenorphine, lorazepam, and carisoprodol, did not produce microcrystals with any of the 37 reagents tested. Further research with these 3 drugs was ceased and did not undergo any additional testing. Phase 2, during which the optical properties of the microcrystals were determined, included the microcrystal test observation and data collection for the new microcrystal tests, specifically crystal morphology, size

color/pleochroism, refractive indices, birefringence, extinction characteristics and sign of elongation. Infrared spectra were also collected for all microcrystal tests that produced positive results. These spectra together with the optical property data will be included in each monograph that is added to the compendium.

Limit of Detection

This project sought to determine each microcrystal test's limit of detection (LOD), or the minimum amount of sample required to obtain a positive result. Many of the reference texts refer to the tests being very sensitive, and some mention a limit of detection using a single crystal the size of a period on a printed page. In order to be as practical and useful as possible for forensic scientists in the laboratory, an analogous unit of measurement was used for this project: throughout the Microcrystal Compendium, sample size is measured in units of PPP, or a "period on a printed page." This unit represents a quantified amount of sample filling the area of a period printed using 10 point font in the Times New Roman style. The estimated weight of a PPP was approximated at about 0.1 mg. All microcrystal tests within the Microcrystal Compendium have LODs from 1PPP up to 5PPP for the drugs analyzed. The LOD is determined using the pure substance and does not reflect the amounts needed when other adulterants, excipients, or drug forms (tablets, liquids, etc.) are used. Nevertheless, it functions as a means to compare relative sensitivities between microcrystal tests, and also gives the lab analyst an indication of required sample quantity.

Refractive Index

The refractive indices of the resulting microcrystals was sometimes a difficult optical property to determine, because the reagent needed to be washed off the crystals and dried before the Cargille certified refractive index liquid could be added for measurement. Crystals in ordinary aqueous reagents were easily dried at room temperature, while those in acidic reagents needed to be washed with a solvent, such as ethanol or chloroform, and dried before their refractive indices could be measured.

In many instances, crystals have refractive index values greater than 1.700. This is a very high refractive index, and above the limit of what most crime laboratories are capable of measuring with their available liquids. Therefore, when samples exhibited a refractive index greater than 1.700, we simply recorded that observation and did not attempt to measure the refractive indices.

Birefringence

Birefringence (B), the numerical difference between principal refractive indices, was determined by estimating the thickness of the crystal using a calibrated ocular scale and applying this measurement to the retardation colors observed between crossed polars. The birefringence value B was then calculated using a Michel-Levy chart of birefringences using the equation, B=R/(1000xT) where R equals retardation and T equals thickness. These B values were reported as low (less than 0.010) or high (greater than 0.050) for the microcrystals that were precipitated by the reactions.

Sign of Elongation

Due to the elongated nature of many of the resulting microcrystals from these tests, a shape-dependent optical property known as sign of elongation was recorded for

identification purposes. When applicable, if the refractive index parallel to a crystal's long axis is greater than the refractive index perpendicular to the long axis, it is a crystal with a positive sign of elongation. If the opposite is true, it has a negative sign of elongation. Some microcrystals have a radial arrangement of a needle-like habit known as a spherulite. In these cases, the sign of elongation test can also be performed, but it is the sign of a spherulite and can also be either positive or negative.

Fourier-Transform Infrared Microspectroscopy

Fourier-transform infrared microspectroscopy (IMS) was used to collect spectra of the resulting crystals obtained during testing. By collecting and including the infrared spectra from all of the resultant microcrystals in the Microcrystal Compendium, microcrystal tests will carry additional weight and build confidence in positively identifying drugs by these alternate techniques.

In reviewing the spectral data, small differences are seen between different microchemical tests for the same drug. These variances may simply be small peak shifts in wavenumbers, but nonetheless constitute distinct differences. The spectra collected from the microcrystals are also different from the spectrum of the original pure drug substance. Thus the chemical reaction that occurs when the microcrystals precipitate out of solution results in an observable change in the resulting spectra.

Adulterants and Excipients

Most of the drugs submitted as evidence to crime laboratories today are not 100% pure substances and may be diluted or cut with adulterants and/or excipients. In addition, pharmaceutical formulations are often mixtures containing multiple drugs, binding agents, fillers, etc. When appropriate, the most commonly encountered

adulterants and excipients were tested in various ratios alongside the drugs to determine the impact on the final microcrystalline form. Usually, the drug of interest was easily identified, even when present in minute quantities compared to a large amount of excipient.

Several types of pharmaceutical tablets were tested to determine whether or not the crystal tests would provide results, including extended-release formulations. In some cases the microcrystal test produced no positive results and micro-scale extractions and concentration of the drug ingredient was required to better facilitate a reaction. After some preparation, most microcrystal tests were successful with pharmaceutical tablets.

4.0 Implications for Criminal Justice Policy and Practice in the US

Microcrystal tests, particularly for drug identification, have been used for so long that many of the tests predate the invention, no less the wide availability of ultraviolet, infrared, or mass spectroscopy and thin layer, liquid, or gas chromatography, as well as other coupled methods that combine one or more of these techniques. This project answers the NAS recommendation for this forensic science discipline to "develop rigorous protocols for performing subjective interpretations" and therefore places a more scientific footing on the evaluation of those crystalline precipitates.

Microcrystal tests are needed to aid in the identification of new and emerging drugs, particularly among crime laboratories that are unable to employ alternate or expensive instrumentation or are not prepared to adapt their instrumentation for less routine analyses. The synthetic cathinones are structurally similar; in some cases, GC-MS may not be able to identify "bath salt" components when more than one active

compound is present because of these close functional similarities. Microcrystal tests, in contrast, are able to exploit these small differences and usually result in the formation of entirely different crystals, allowing for differentiation and identification, even among isomers. Microcrystal tests are fast, relatively easy to conduct, and require few supplies beyond reagents and a microscope, with which most forensic laboratories are equipped. These tests would therefore be fairly simple to incorporate into current laboratory protocols.

The original Microcrystal Compendium published in 2015, which was authored by McCrone Research Institute and funded by a grant from the NIJ, has already gained popularity and has had a significant impact within the criminal justice system. As an example, the Minnesota Bureau of Criminal Apprehension (BCA) was able to implement microcrystal testing for cocaine, heroin, and methamphetamine. Within a six-month period of time they were able to entirely eliminate their backlog. This has been particularly helpful with plea agreements and the Minnesota BCA received a "Better Government Award" for customer service from their Governor. Microcrystal testing is now done in 70% of Minnesota counties; it is also estimated that 70% of BCA submissions are eligible for microcrystal testing.

The significance and magnitude of providing analysts with new, updated, and validated scientific methods for the identification of illicit drugs and pharmaceuticals cannot be overstated, and it is hoped that the addition of tests for controlled drugs, diverted pharmaceuticals, and bath salts to McCrone Research Institute's Modern Compendium of Microcrystal Tests will have a profound impact on the criminal justice field.

APPENDIX: NIJ FINAL SUMMARY OVERVIEW

Development of Modern Microcrystal Tests for Controlled Drugs, Diverted Pharmaceuticals, and Bath Salts

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Alprazolam: Gold Bromide with Hydrochloric Acid

REAGENT 1A: Gold Bromide ($HAuBr_4$) with Concentrated Hydrochloric Acid (HCl)

There are two ways to make this reagent: 1.3 g $HAuBr_4$ in concentrated HCl, make up to 30 mL. Alternatively, to convert gold chloride to gold bromide: 1 g $HAuCl_4 \cdot 3H_2O$ and 1.5 mL HBr (40%) in concentrated HCl, make up to 30 mL. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Dissolve sample in 2 µL of 10% HCl. Place a 5 µL drop of reagent on a coverslip. Invert the coverslip and place it directly onto the dissolved sample. Or, dissolve sample in 5 µL of 10% HCl, then add 5 µL of reagent and gently mix drop with pipette tip, glass rod, or toothpick to induce crystallization.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈9 minutes (pharmaceuticals up to ≈20 minutes).

Crystal Morphology and Test Notes

Curved, wispy rosettes. Crystals also form clusters of straight needles and blades.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of alprazolam in 2 µL of 10% HCl and 5 µL of $HAuBr_4$ with HCl reagent. Crystals form curved, wispy rosettes.

Pharmaceuticals, Adulterants, or Other Drug Interactions

These tests were successful on four different alprazolam pharmaceutical tablets and an alprazolam oral solution. Different procedures were necessary for successful results.

Acid-base extraction procedure, tablet. Tests of pharmaceutical tablets from two different manufacturers were successful after an acid-base extraction procedure: crush a small portion of tablet material and place it in a microcentrifuge tube. Add 500 µL of 10% H_2SO_4 and mix by aspirating with a transfer pipette. Slowly add 500 µL of saturated Na_2CO_3 solution and mix, then add 50 µL of chloroform and mix. Use a micropipette to decant 10 µL from the chloroform layer (bottom) onto a glass slide. Allow to evaporate, then proceed with microcrystal test. These tests were successful with the tablets in the following

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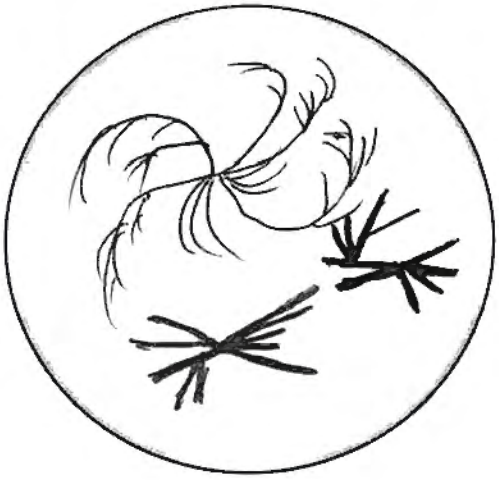
PLM Optical Properties

Approximate Size Range	25–100 µL
Color/Pleochroism	Yellow-orange. Pleochroic: yellow to dark yellow-orange.
Refractive Indices (RI)	n-parallel ≈ 1.700 n-perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique (≈40°)
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Alprazolam: Gold Bromide with Hydrochloric Acid (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

required quantities:

- ½ tablet Sandoz® 0.25 mg alprazolam
- 1 tablet Actavis® 0.25 mg alprazolam
- ⅛ tablet Sandoz® 2.0 mg alprazolam

Note: Typical crystals form within 15–20 minutes.

Ethanol extraction procedure, extended release tablet. A test of a Greenstone® 0.5 mg extended release tablet was successful after an ethanol extraction procedure: place ½ tablet into a microcentrifuge tube with 1 mL of ethanol and allow to sit for 30 minutes, then centrifuge. Use a micropipette to decant 20 µL onto a glass slide, then proceed with test method. Note: Typical crystals form within 15–20 minutes.

Chloroform extraction procedure, oral solution. A test of an Intensol® oral solution containing 1 mg/mL of alprazolam was successful after a chloroform extraction: Transfer 100 µL of the oral solution into a microcentrifuge tube, add dilute NH_4OH to pH 9, then shake. Add 100 µL of chloroform and shake vigorously. Allow to separate, then use a micropipette to remove and transfer the chloroform/alprazolam (bottom) layer into a clean microcentrifuge tube. Adjust to pH 6 with 10% HCl and shake. Use a micropipette to decant 10 µL onto a glass slide, then proceed with test method. Note: Typical crystals form within 15–20 minutes.

IR Spectrum

See Figure 10. Download/view SPC file

Figure 2. 1 PPP of alprazolam in 2 µL of 10% HCl and 5 µL of reagent: $HAuBr_4$ in HCl. Crystals form curved, wispy rosettes and clusters of straight needles and blades.

Figure 3. 1 PPP of alprazolam in 2 µL of 10% HCl and 5 µL of reagent: $HAuBr_4$ in HCl. Crystals form curved, wispy rosettes and clusters of straight needles.

Figure 4. 1 PPP of alprazolam in 2 µL of 10% HCl and 5 µL of reagent: $HAuBr_4$ in HCl. Crystals form curved, wispy rosettes and clusters of straight needles and blades.

Figure 5. ½ of a Sandoz® 0.25 mg tablet, after acid-base extraction procedure. Crystals form curved, wispy rosettes and clusters of straight needles and blades in 20 minutes.

Alprazolam: Gold Bromide with Hydrochloric Acid (continued)

Figure 6. ⅛ of a Sandoz® 2.0 mg tablet after acid-base extraction procedure. Crystals form curved, wispy rosettes in 16 minutes.

Figure 8. 1 Actavis® 0.25 mg tablet after acid-base extraction procedure. Crystals form curved, wispy rosettes in 15 minutes.

Figure 7. ½ of a Greenstone® 0.5 mg extended release tablet after ethanol extraction procedure. Crystals form curved, wispy rosettes in 20 minutes.

Figure 9. 100 µL from a 1 mg/mL Intensol® alprazolam oral solution after chloroform extraction procedure. Crystals form curved, wispy rosettes in 15 minutes.

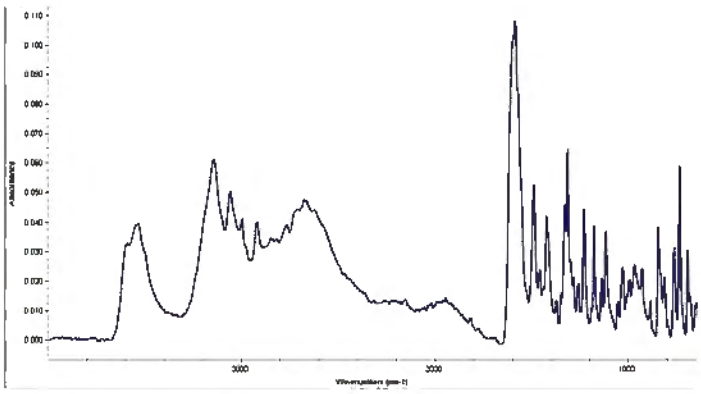


Figure 10. Infrared spectrum of alprazolam gold bromide with concentrated hydrochloric acid precipitate.
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Alprazolam: Gold Bromide with Sulfuric Acid and Acetic Acid

REAGENT 1B: Gold Bromide ($HAuBr_4$) with Sulfuric Acid (H_2SO_4) and Acetic Acid (HOAc)

There are two ways to make this reagent: 1.3 g $HAuBr_4$ in (2+3) H_2SO_4, make up to 30 mL. (2+3) H_2SO_4 is dilute sulfuric acid made by combining two parts (e.g. 12 mL) of concentrated sulfuric acid with three parts (e.g. 18 mL) of water. Then add 10 mL of glacial HOAc. Alternatively, to convert gold chloride to gold bromide: 1 g $HAuCl_4 \cdot 3H_2O$ and 1.5 mL HBr (40%) in (2+3) H_2SO_4, make up to 30 mL. Then add 10 mL of glacial HOAc.

Test Method

Direct test: Place sample on glass slide. Add a 5 µL drop of reagent on coverslip, invert the coverslip, and place it directly onto the sample. Alternatively, add 5 µL of the reagent directly to the sample on a glass slide; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈8 minutes (pharmaceuticals up to ≈15 minutes).

Crystal Morphology and Test Notes

Wispy rosettes of needles and blades. Crystals also form burrs, fans, and sheaves.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of alprazolam in 5 µL of $HAuBr_4$ with H_2SO_4 and HOAc reagent. Crystals form rosettes of needles and blades, burrs, fans, and sheaves.

Pharmaceuticals, Adulterants, or Other Drug Interactions

These tests were successful on four different alprazolam pharmaceutical tablets and an alprazolam oral solution. Different procedures were necessary for successful results.

Acid-base extraction procedure, tablet. Tests of pharmaceutical tablets from two different manufacturers were successful after an acid-base extraction procedure: crush a small portion of tablet material and place it in a microcentrifuge tube. Add 200 µL of 10% H_2SO_4 and mix by aspirating with a transfer pipette. Slowly add 200 µL of saturdated Na_2CO_3 solution and mix, then add 50 µL of chloroform and mix. Use a micropipette to draw off 10 µL from the chloroform layer (bottom) and place a small drop onto a glass slide (it does not need to evaporate) and

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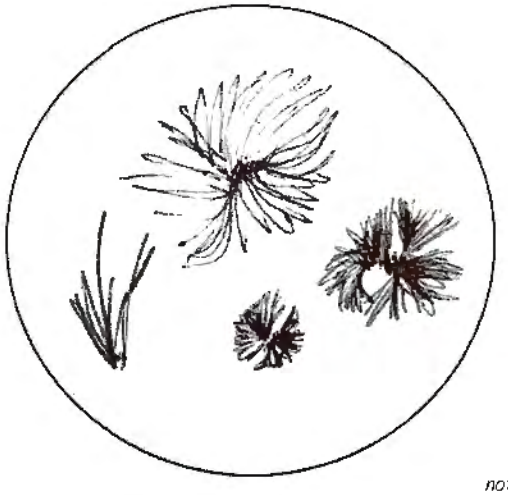
PLM Optical Properties

Approximate Size Range	20–100 µL
Color/Pleochroism	Yellow-orange. Pleochroic: yellow to dark yellow-orange.
Refractive Indices (RI)	n > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique (≈40°)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Alprazolam: Gold Bromide with Sulfuric Acid and Acetic Acid (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

proceed with the microcrystal test. These tests were successful with the tablets in the following required quantities:

- ½ tablet Sandoz® 0.25 mg alprazolam
- ½ tablet Actavis® 0.25 mg alprazolam
- ¼ tablet Sandoz® 2.0 mg alprazolam

Note: Typical crystals form within 10–15 minutes.

Ethanol extraction procedure, extended release tablet. A test of a Greenstone® 0.5 mg extended release tablet was successful after an ethanol extraction procedure: place ½ tablet into a microcentrifuge tube with 1 mL of ethanol and allow to sit for 30 minutes, then centrifuge. Use a micropipette to decant 20 µL onto a glass slide, then proceed with test method. Note: Typical crystals form within 10–15 minutes.

Chloroform extraction procedure, oral solution. A test of an Intensol® oral solution containing 1 mg/mL of alprazolam was successful after a chloroform extraction: Transfer 100 µL of the oral solution into a microcentrifuge tube, add dilute NH_4OH to pH 9, then shake. Add 100 µL of chloroform and shake vigorously. Allow to separate, then use a micropipette to remove and transfer the chloroform/alprazolam (bottom) layer into a clean microcentrifuge tube. Adjust to pH 6 with 10% HCl and shake. Use a micropipette to decant 10 µL onto a glass slide, then proceed with test method. Note: Typical crystals form within 10–15 minutes.

IR Spectrum

See Figure 9. Download/view SPC file

Figure 2. 1 PPP of alprazolam in 5 µL of $HAuBr_4$ with H_2SO_4 and HOAc reagent. Crystals form wispy rosettes of needles and blades.

Figure 3. 1 PPP of alprazolam in 5 µL of $HAuBr_4$ with H_2SO_4 and HOAc reagent. Crystals form wispy rosettes of needles and blades.

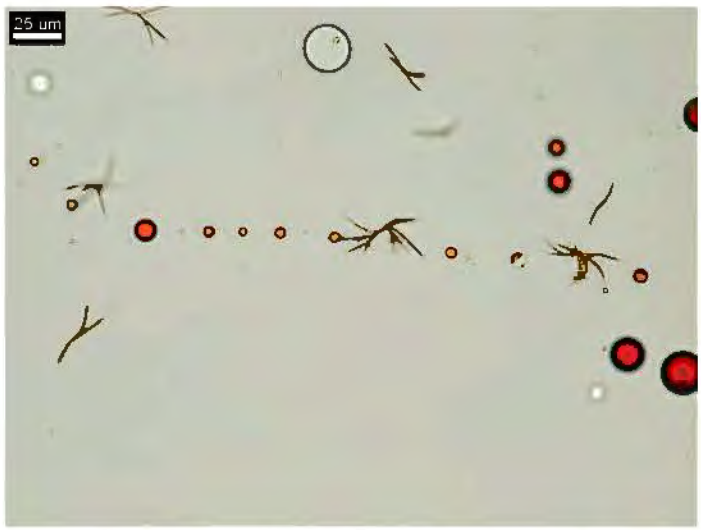


Figure 4. ½ of a Sandoz® 0.25 mg tablet after acid-base extraction procedure. Crystals form wispy rosettes of needles and blades in 10 minutes.

Figure 5. ¼ of a Sandoz® 2.0 mg tablet after acid-base extraction procedure. Crystals form wispy rosettes of needles in 11 minutes.

Alprazolam: Gold Bromide with Sulfuric Acid and Acetic Acid (continued)

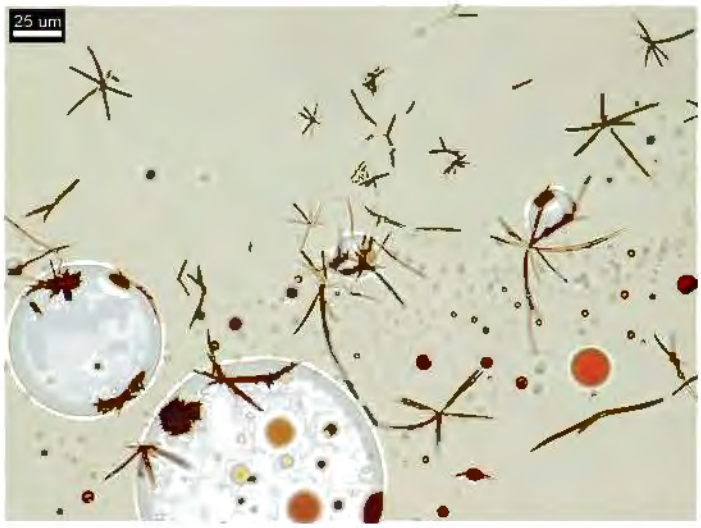


Figure 6. ½ of 0.25 mg Actavis® tablet after acid-base extraction procedure. Crystals form wispy rosettes of needles and blades in 15 minutes.

Figure 7. ½ of a Greenstone® 0.5 mg extended release tablet after ethanol extraction procedure. Crystals form wispy rosettes of needles and blades in 15 minutes.

Figure 8. 100 µL from a 1 mg/mL Intensol® alprazolam oral solution after chloroform extraction procedure. Crystals form curved, wispy rosettes in 15 minutes.

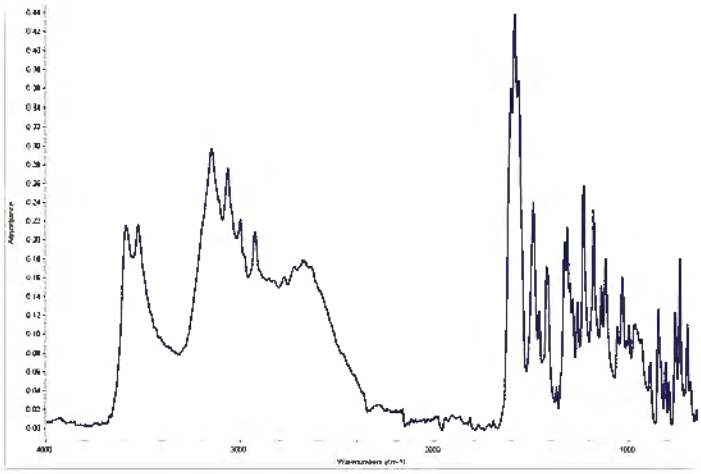


Figure 9. Infrared spectrum of alprazolam gold bromide with sulfuric acid and acetic acid precipitate. Download/view SPC file

Butylone: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP (A larger amount of sample results in faster and larger crystal growth.)

Time Required for Crystal Formation

≈3 minutes

Crystal Morphology and Test Notes

Rosettes of tablets.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of butylone in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of tablets.

Pharmaceuticals, Adulterants or Other Drug Interactions

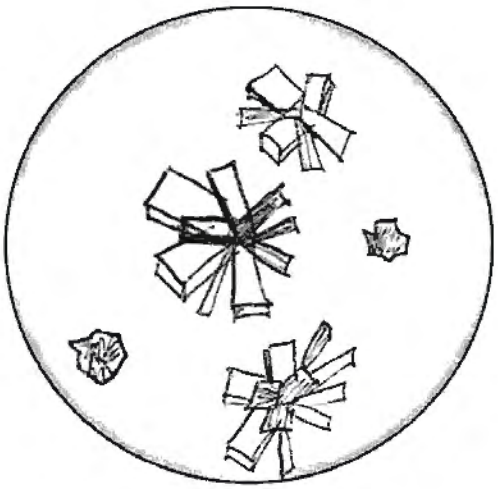
Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of butylone with selected adulterants is listed below:

- 4-MEC:butylone — detectable at 1:5, 1:1, and 5:1
- Alpha-PVP:butylone — detectable at 1:5, 1:1, and 5:1
- BZP:butylone — detectable at 1:5, 1:1, and 5:1
- Caffeine:butylone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:butylone — detectable at 1:5, 1:1, and 5:1
- MDPV:butylone — detectable at 1:5, 1:1, and 5:1
- Mephedrone:butylone — detectable at 1:5, 1:1, and 5:1
- Methylone:butylone — detectable at 1:5, 1:1, and 5:1
- TFMPP:butylone — detectable at 1:5, 1:1, and 5:1

IR Spectrum

See Figure 6. Download/view SPC file

PLM Optical Properties

Approximate Size Range	10–115 µm
Color/Pleochroism	Yellow-brown. Pleochroic: dark brown to light yellow
Refractive Indices (RI)	$n_1 \approx 1.500$ $n_2 > 1.700$
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique (individual tablets) and parallel
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Butylone: Palladium Chloride with HCl and H_3PO_4 (continued)

Figure 2. 1 PPP of butylone in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of tablets.

Figure 3. 1 PPP of butylone in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of tablets.

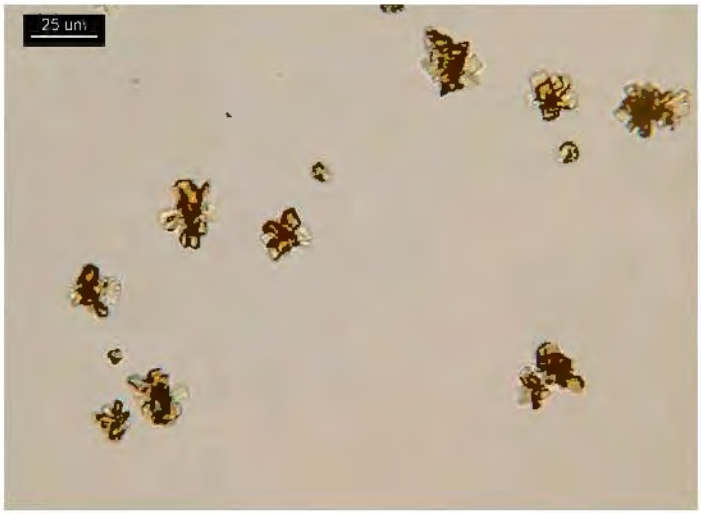


Figure 4. Methylone:butylone mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of tablets.

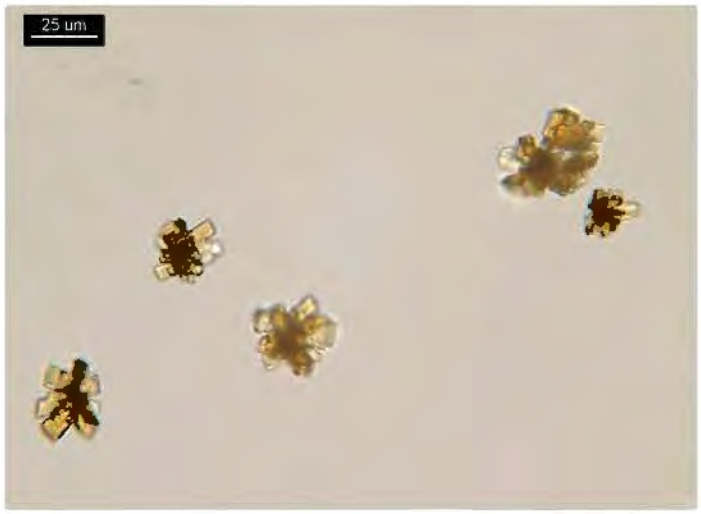


Figure 5. 4-MEC:butylone mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of tablets.

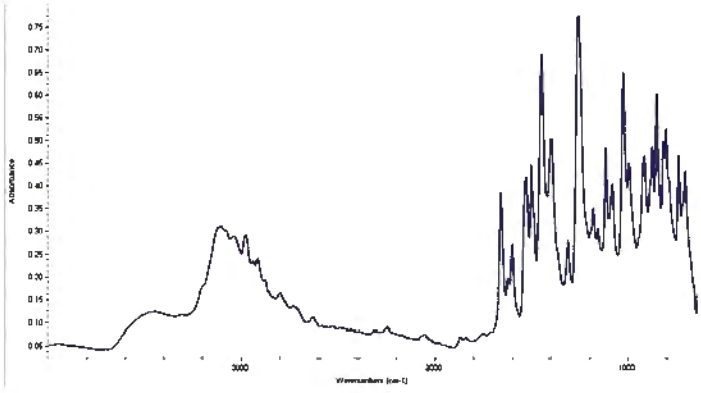


Figure 6. Intrared spectrum of butylone palladium chloride with HCl and H_3PO_4 precipitate. Download/view SPC file.

Butylone: Platinum Bromide with Sulfuric Acid

REAGENT 2: Platinum Bromide (H_2PtBr_6) with Sulfuric Acid ((2+3) H_2SO_4)

There are two ways to make this reagent: 1.3 g H_2PtBr_6 in (2+3) H_2SO_4, make up to 20 mL. (2+3) H_2SO_4 is dilute sulfuric acid made by combining two parts (e.g. 8 mL) of concentrated sulfuric acid with three parts (e.g. 12 mL) of water. Alternatively, to convert platinum chloride to platinum bromide: 1 g $H_2PtCl_6 \cdot 6H_2O$ and 1.7 mL HBr (40%) in (2+3) H_2SO_4, make up to 20 mL.

Test Method

Direct test: Add 5 µL of reagent directly to sample; with or without coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP (A larger amount of sample results in faster and larger crystal growth.)

Time Required for Crystal Formation

≈2–5 minutes

Crystal Morphology and Test Notes

Coffin lid-shaped tablets and rosettes of tablets with coverslip and rectangular tablets and rosettes of tablets without coverslip.

Photomicrograph of Typical Crystals

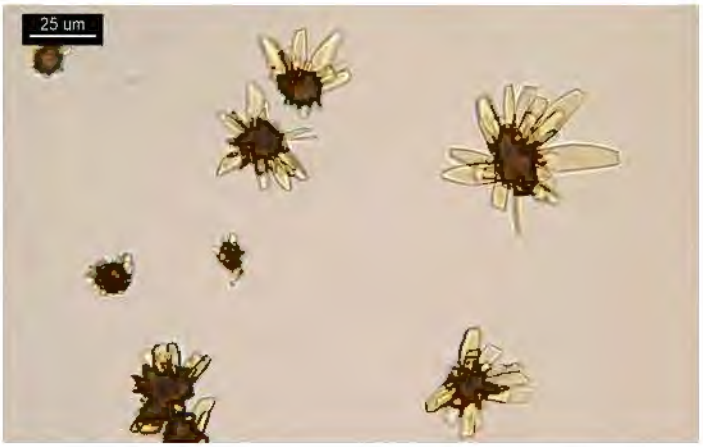


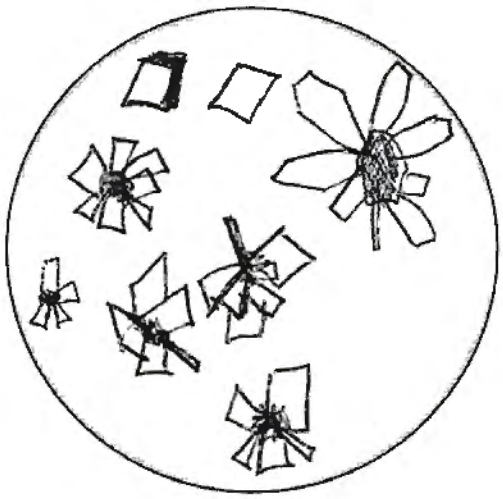
Figure 1. 1 PPP of butylone in 5 µL of H_2PtBr_6 with (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped tablets and rosettes of tablets.

Pharmaceuticals, Adulterants or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of butylone with selected adulterants is listed below:

- 4-MEC:butylone — detectable at 1:5, 1:1, and 5:1
- Alpha-PVP:butylone — detectable at 1:5, 1:1, and 5:1
- BZP:butylone — detectable at 1:5, 1:1, and 5:1
- Caffeine:butylone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:butylone — detectable 1:5; undetectable at 1:1 and 5:1
- MDPV:butylone — detectable at 1:5 and 1:1; undetectable at 5:1
- Mephedrone:butylone — detectable at 1:5; undetectable at 1:1 and 5:1.
- Methylone:butylone — detectable at 1:5, 1:1, and 5:1
- TFMPP:butylone — detectable at 1:5, 1:1, and 5:1

PLM Optical Properties

Approximate Size Range	10–60 µm
Color/Pleochroism	Yellow; not pleochroic
Refractive Indices (RI)	$n_1 = 1.700$ $n_2 > 1.700$
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with water and dried with gentle heat.
Estimated Birefringence	High
Extinction	Oblique (individual tablets) and parallel
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Butylone: Platinum Bromide with Sulfuric Acid (continued)

Figure 2. 1 PPP of butylone in 5 µL of H_2PtBr_6 with (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped tablets and rosettes of tablets.

Figure 3. 1 PPP of butylone in 5 µL of H_2PtBr_6 with (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped tablets and rosettes of tablets.

Figure 4. 1 PPP of butylone in 5 µL of H_2PtBr_6 with (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets.

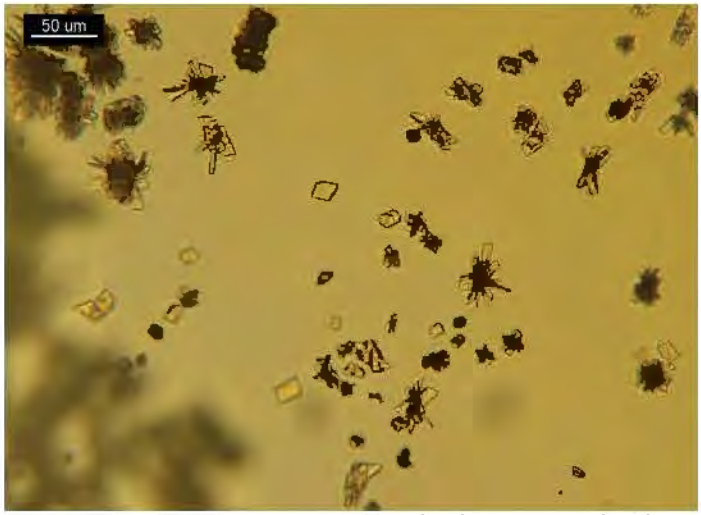


Figure 5. Alpha-PVP:butylone mixture (5:1) and 5 µL of (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets.

Butylone: Platinum Bromide with Sulfuric Acid (continued)

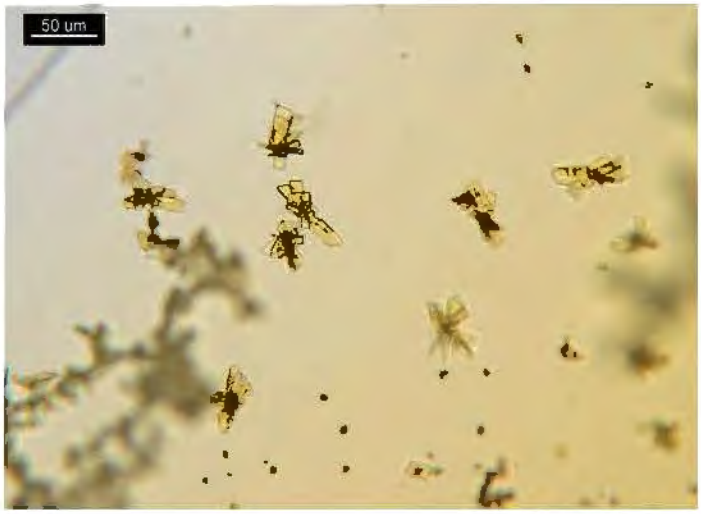


Figure 6. BZP:butylone mixture (1:1) and 5 µL of (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets.

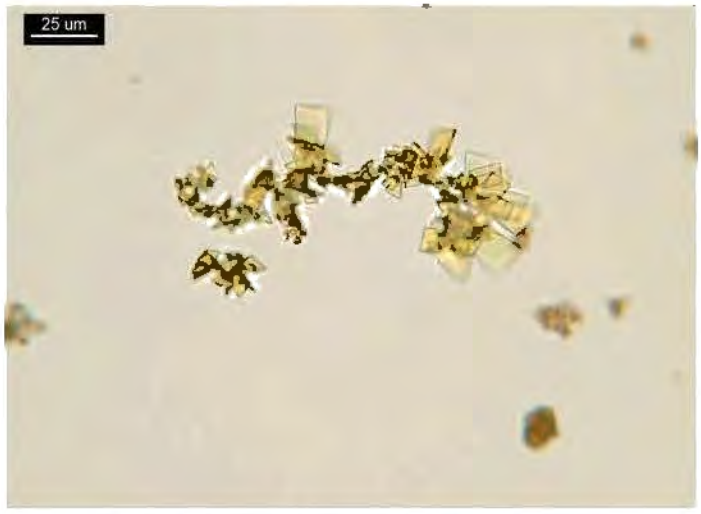


Figure 7. Caffeine:butylone mixture (5:1) and 5 µL of (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets.

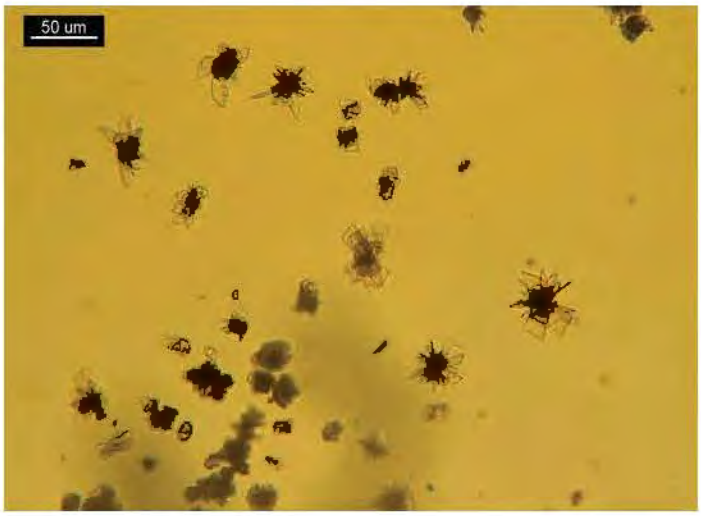


Figure 8. Lidocaine HCl:butylone mixture (1:5) and 5 µL of (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets with distortions.

Figure 9. TFMPP:butylone mixture (5:1) and 5 µL of (2+3) H_2SO_4 reagent. Crystals form coffin lid-shaped and rectangular tablets and rosettes of tablets.

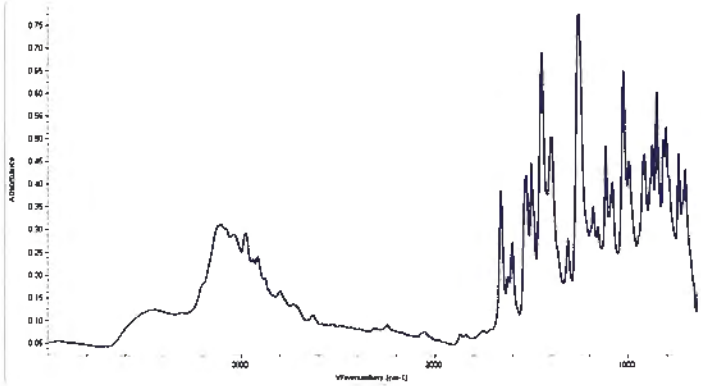


Figure 10. Infrared spectrum of butylone platinum bromide with sulfuric acid precipitate. Download/view SPC file

MDPV*: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP (5 PPP for most common adulterants)

Time Required for Crystal Formation

1–5 minutes (adulterants up to ≈20 minutes)

Crystal Morphology and Test Notes

Burrs and platey burrs

Photomicrograph of Typical Crystals

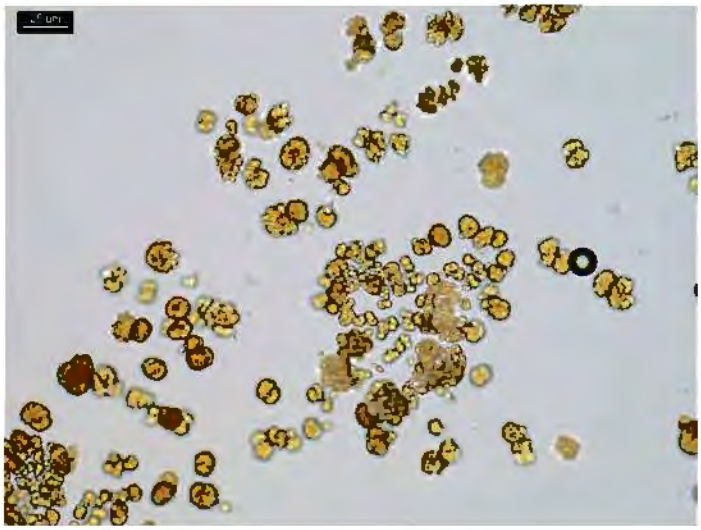


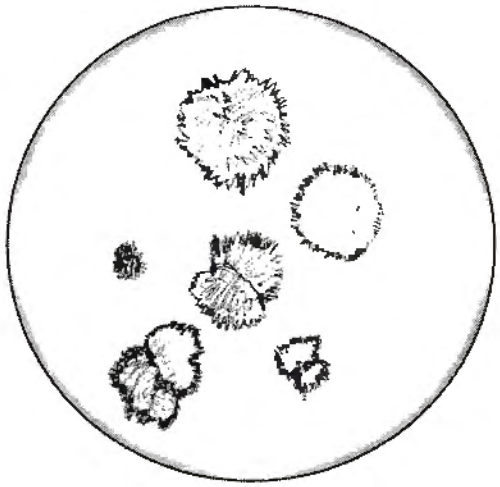
Figure 1. 1 PPP of MDPV in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form burrs and platey burrs.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, butylone, BZP, caffeine, ethylone, lidocaine HCl, mephedrone, methylone, and TFMPP. The detectability of MDPV with selected adulterants is listed below:

- 4-MEC:MDPV — detectable at 1:5, 1:1, and 5:1
- Alpha-PVP:MDPV — detectable at 1:5, 1:1, and 5:1
- Butylone:MDPV — detectable at 1:5; undetectable at 1:1 and 5:1
- BZP:MDPV — detectable at 1:5, 1:1, and 5:1
- Caffeine:MDPV — detectable at 1:5, 1:1, and 5:1
- Ethylone:MDPV — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:MDPV detectable at 1:5, 1:1, and 5:1
- Mephedrone:MDPV detectable at 1:5, 1:1; undetectable at 5:1
- Methylone:MDPV — detectable at 1:5, 1:1, and 5:1
- TFMPP:MDPV — detectable at 1:5, 1:1, and 5:1

PLM Optical Properties

Approximate Size Range	5–40 µm
Color/Pleochroism	Dark yellow; not pleochroic
Refractive Indices (RI)	n ≈1.660 Crystals are slightly soluble in RI liquids.
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Polycrystalline
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

*MDPV is another name for methylenedioxypyrovalerone.

MDPV: Palladium Chloride with HCl and H_3PO_4 (continued)

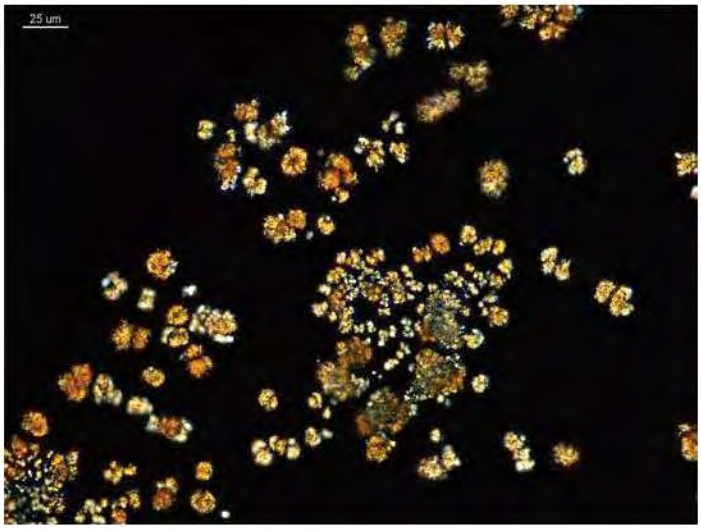


Figure 2. Same as Figure 1; crossed polars.

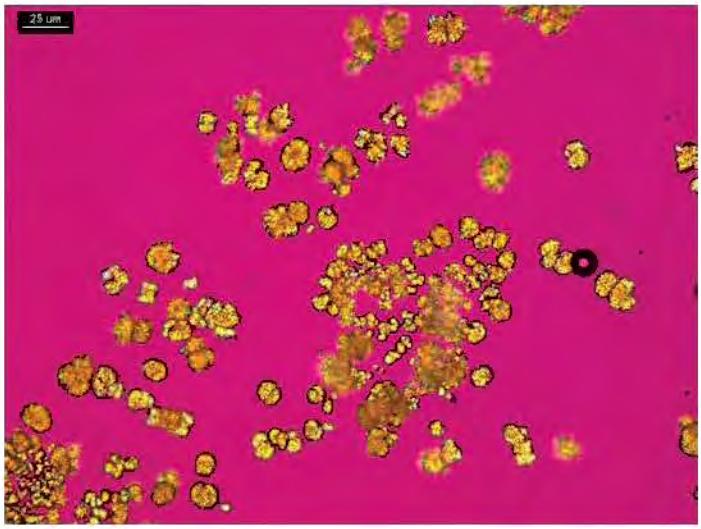


Figure 3. Same as Figure 1; crossed polars and Red I compensator.

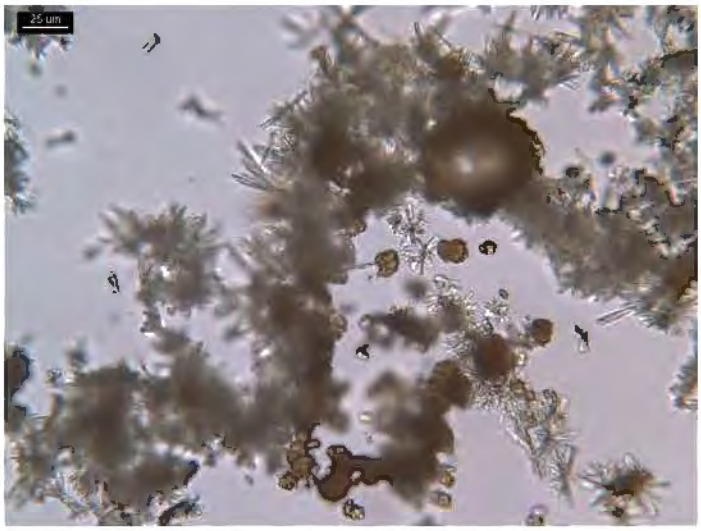


Figure 4. BZP:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

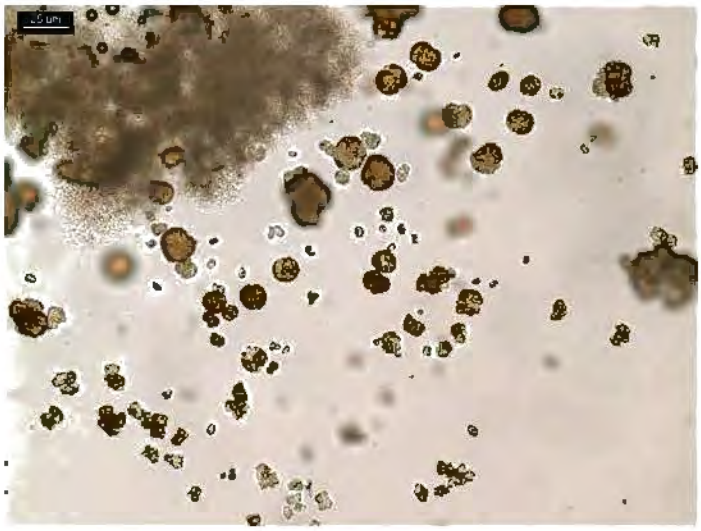


Figure 5. Caffeine:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

MDPV: Palladium Chloride with HCl and H_3PO_4 (continued)

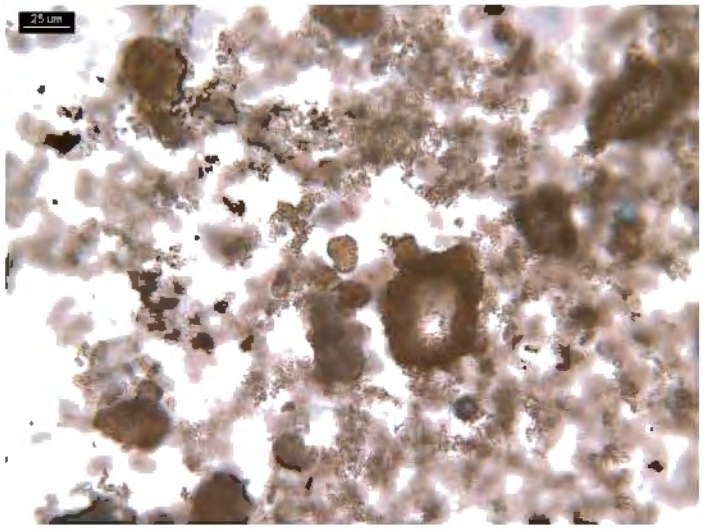


Figure 6. Ethylone:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

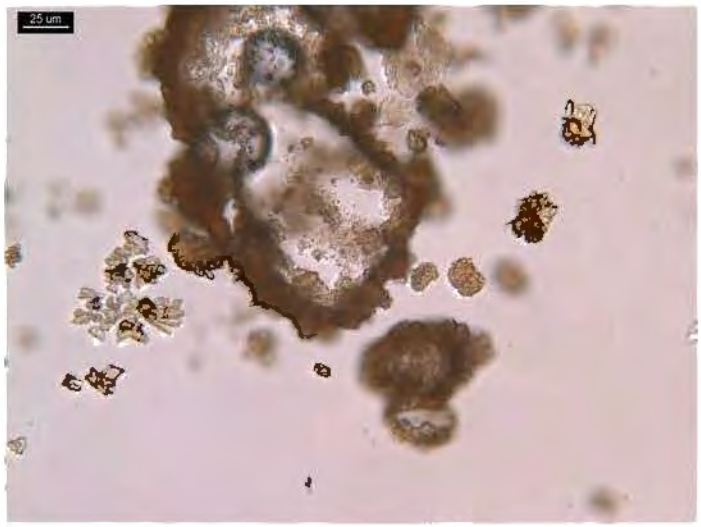


Figure 7. Lidocaine HCl:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

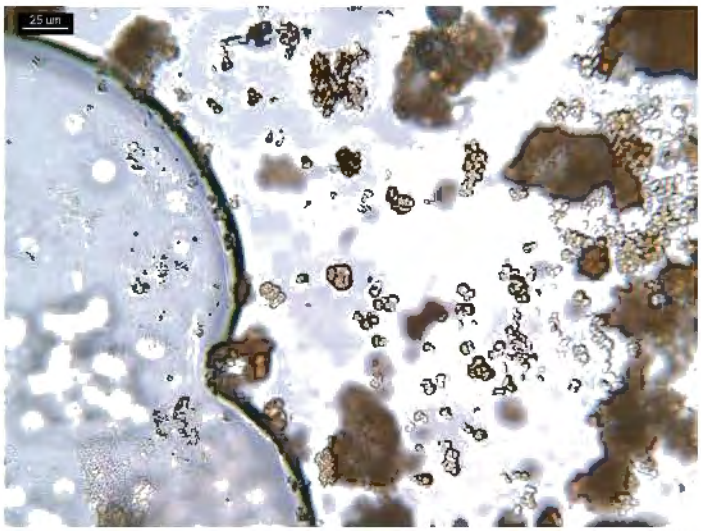


Figure 8. Mephedrone:MDPV mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

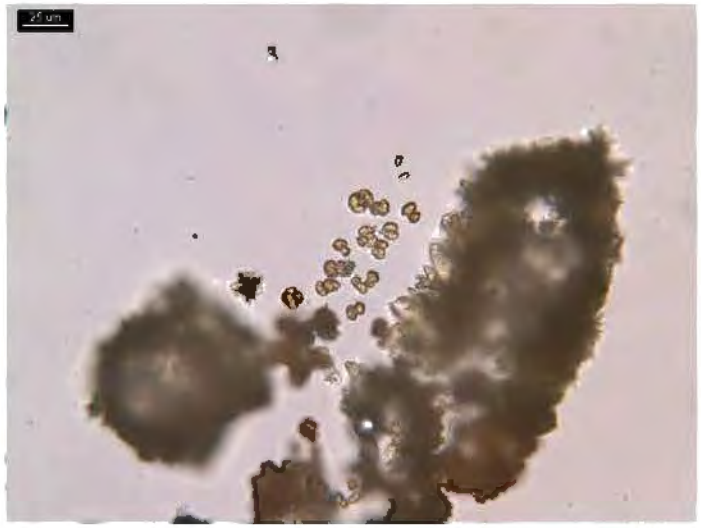


Figure 9. Methylone:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

MDPV: Palladium Chloride with HCl and H_3PO_4 (continued)

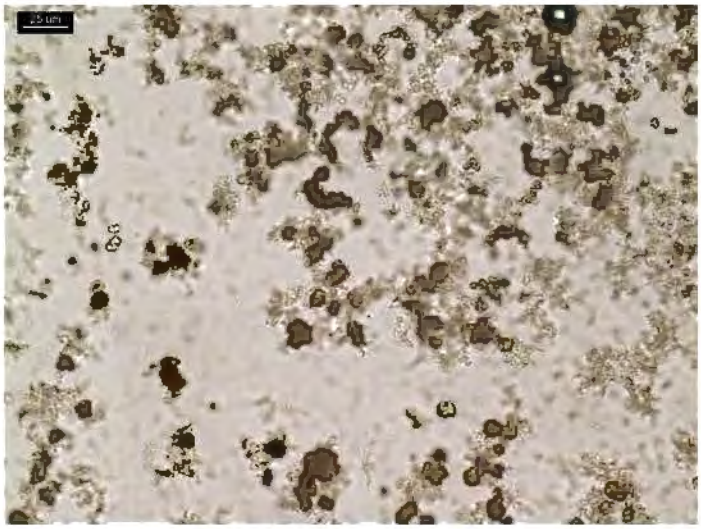


Figure 10. TFMPP:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

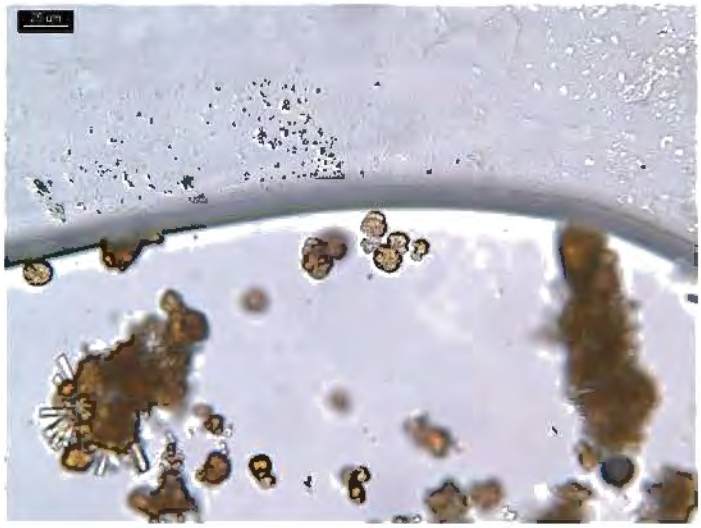


Figure 11. 4-MEC:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

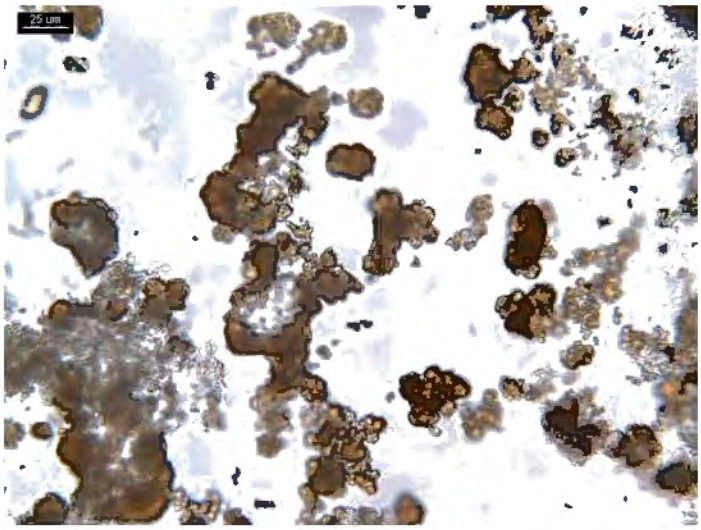


Figure 12. Alpha-PVP:MDPV mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form dark yellow burrs and platey burrs.

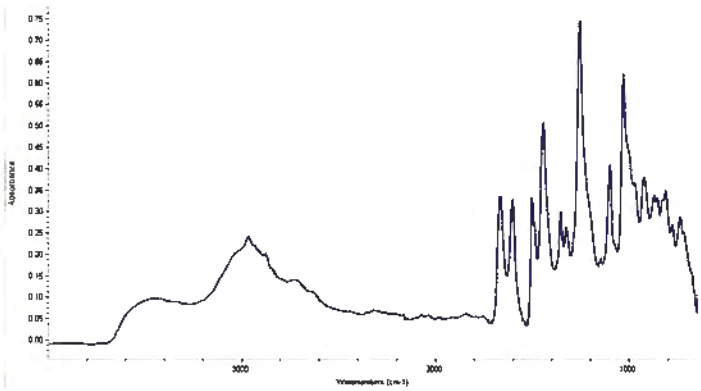


Figure 13. Infrared spectrum of MDPV palladium chloride with HCl and H_3PO_4 precipitate. Download/view SPC file

MDPV: Gold Bromide with Phosphoric Acid and Acetic Acid

REAGENT 2: Gold Bromide ($HAuBr_4$) with Concentrated Phosphoric Acid (H_3PO_4) and Acetic Acid (HOAc)

$HAuBr_4$ in H_3PO_4· 5HOAc. To convert gold chloride to gold bromide: 1 g $HAuCl_4 \cdot 3H_2O$ and 1.5 mL HBr (40%). Then add of 8 mL concentrated H_3PO_4 and 40 mL glacial HOAc. Note: This test method also requires (1+2) H_3PO_4, which is dilute phosphoric acid made by combining one part (e.g. 6.67 mL) of concentrated phosphoric acid with two parts (e.g. 13.33 mL) of water.

Test Method

Direct test: Dissolve sample in 2 µl of (1+2) H_3PO_4. Add a 5 µL drop of reagent on coverslip, invert the coverslip, and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

2 PPP

Time Required for Crystal Formation

5–10 minutes

Crystal Morphology and Test Notes

Clusters of platey dendrites.

Photomicrograph of Typical Crystals

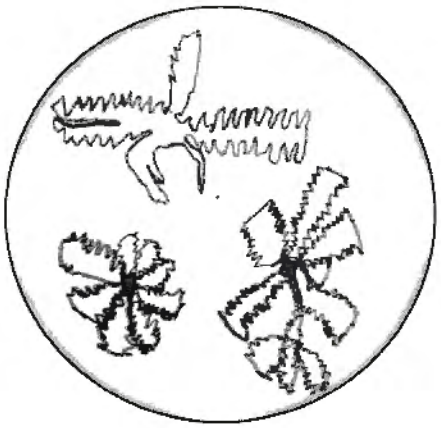
Figure 1. 2 PPP of MDPV in 2 µL of (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with $H_3PO_4$and HOAc reagent. Crystals form platey dendrites.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, butylone, BZP, caffeine, ethylone, lidocaine HCl, mephedrone, methylone, and TFMPP. The detectability of MDPV with selected adulterants is listed below:

- 4-MEC:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Alpha-PVP:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Butylone:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- BZP:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Caffeine:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Ethylone:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Lidocaine HCl:MDPV—detectable at 1:5; undetectable at 1:1 and 5:1
- Mephedrone:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1
- Methylone:MDPV— detectable at 1:5 and 1:1; undetectable at 5:1
- TFMPP:MDPV—detectable at 1:5 and 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	100–700 µm
Color/Pleochroism	Yellow. Pleochoic: Dark yellow (parralel) to yellow (perpendicular)
Refractive Indices (RI)	≈1.700 and >1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	Moderate–High
Extinction	Polycrystalline
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

MDPV: Gold Bromide (continued)

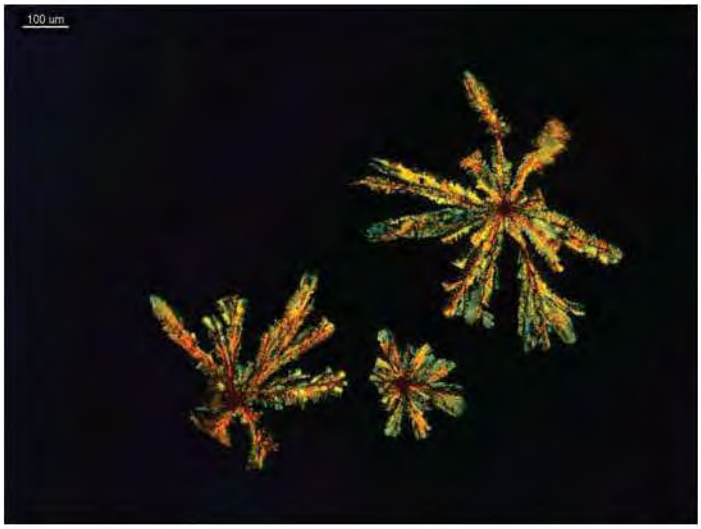


Figure 2. Same as Figure 1; crossed polars.

Figure 3. Same as Figure 1; crossed polars and Red I compensator.

Figure 4. 2 PPP of MDPV in 2 µL of (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 5. 4-MEC:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

MDPV: Gold Bromide (continued)

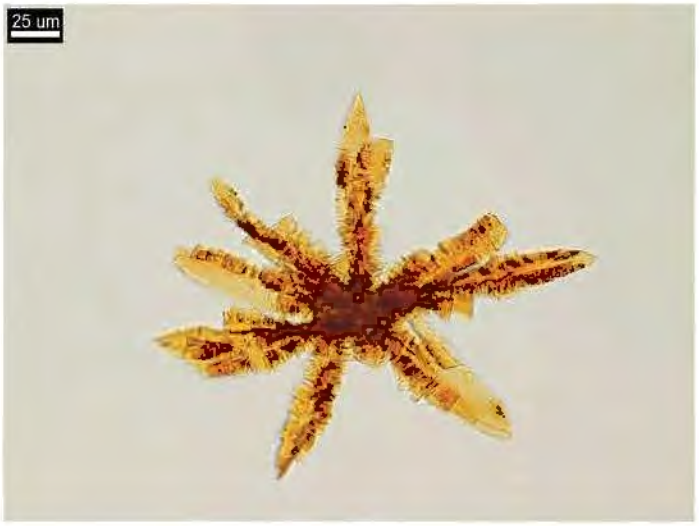


Figure 6. Alpha-PVP:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

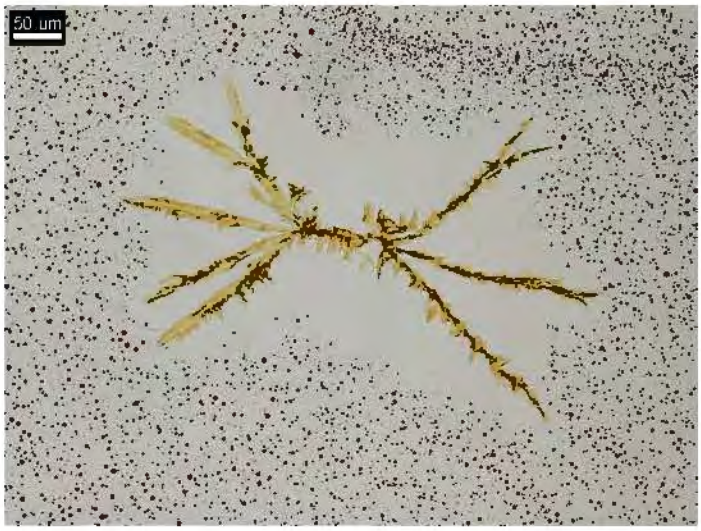


Figure 7. 4-MEC:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 8. BZP:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 9. Caffeine:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

MDPV: Gold Bromide (continued)

Figure 10. Ethylone:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 11. Mephedrone:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 12. Methylone:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

Figure 13. TFMPP:MDPV mixture (1:1) in 2 µL (1+2) H_3PO_4 and 5 µL of $HAuBr_4$ with H_3PO_4 and HOAc reagent. Crystals form platey dendrites.

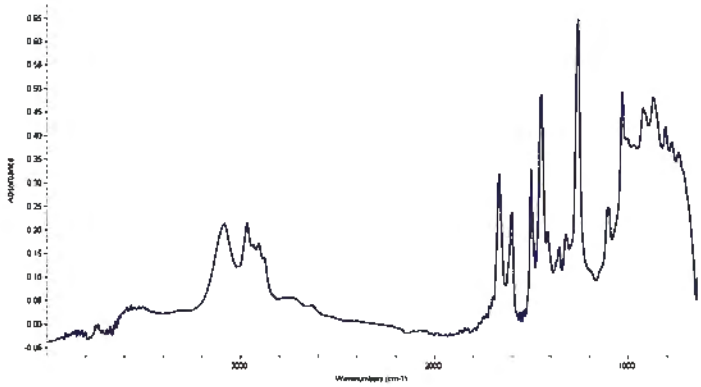


Figure 14. Infrared spectrum of MDPV gold bromide with H_3PO_4 and HOAc reagent precipitate. Download/view SPC file

4-MEC*: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

1–5 minutes

Crystal Morphology and Test Notes

Rosettes of blades and rods, sometimes feathery.

Photomicrograph of Typical Crystals

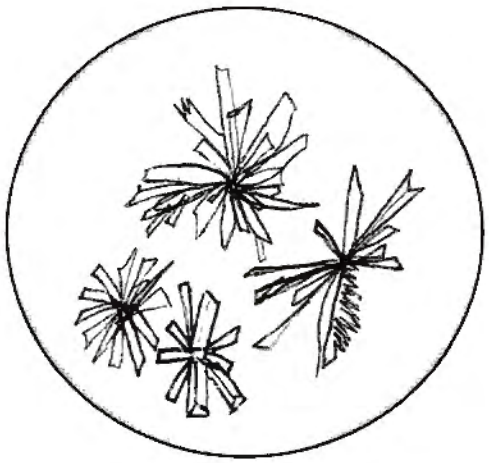
Figure 1. 1 PPP of 4-MEC in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of blades and rods, sometimes feathery.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include alpha-PVP, butylone, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of 4-MEC with selected adulterants is listed below:

- Alpha-PVP:4-MEC — detectable at 1:5; undetectable at 1:1 and 5:1
- BZP:4-MEC — detectable at 1:5; undetectable at 1:1 and 5:1
- Butylone:4-MEC — detectable at 1:5 and 1:1; undetectable at 5:1
- Caffeine:4-MEC — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:4-MEC — detectable at 1:5; undetectable at 1:1 and 5:1
- MDPV:4-MEC — detectable at 1:5, 1:1, and 5:1
- Mephedrone:4-MEC — detectable at 1:5, 1:1; undetectable at 5:1
- Methylone:4-MEC — detectable at 1:5; undetectable at 1:1 and 5:1
- TFMPP:4-MEC — detectable at 1:5 and 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	Rosettes: 10–100 µm Individual blades: 1–5 µm width
Color/Pleochroism	Yellow. Pleochroic: light yellow to yellow (perpendicular); may not be apparent on some crystals.
Refractive Indices (RI)	n-parallel ≈ 1.700 n-perpendicular ≈ 1.510
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed in absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique and parallel
Sign of Elongation	Mostly positive (+) and some negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

*4-MEC is another name for 4-Methylethcathinone.

4-MEC: Palladium Chloride with HCl and H_3PO_4 (continued)

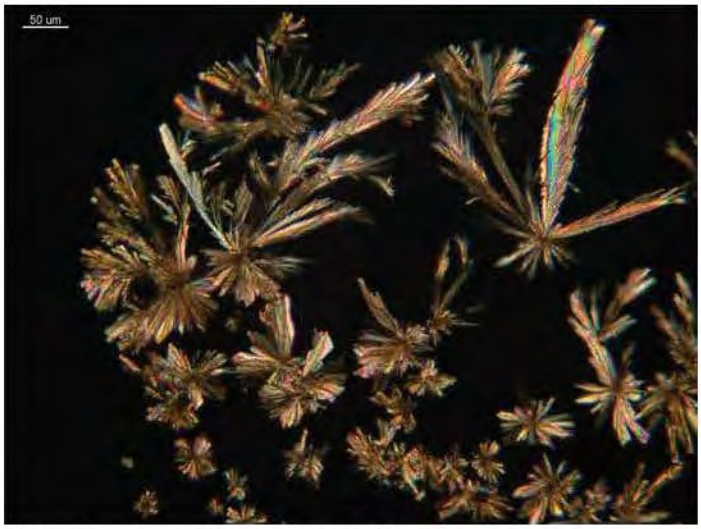


Figure 2. Same as Figure 1; crossed polars.

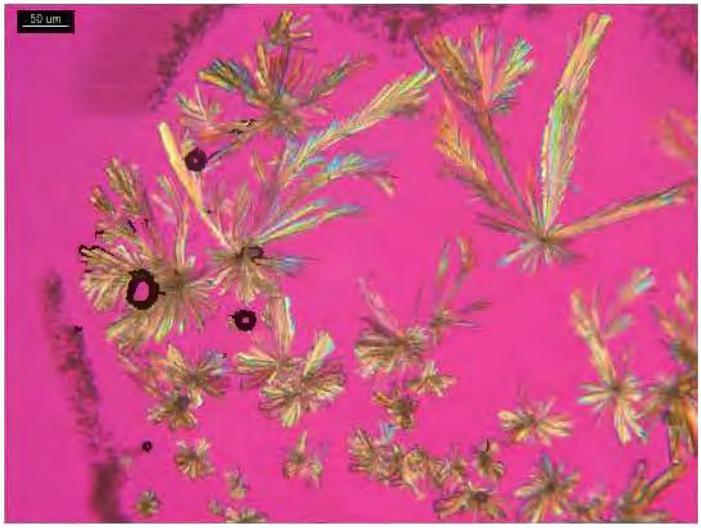


Figure 3. Same as Figure 1; crossed polars and Red I compensator.

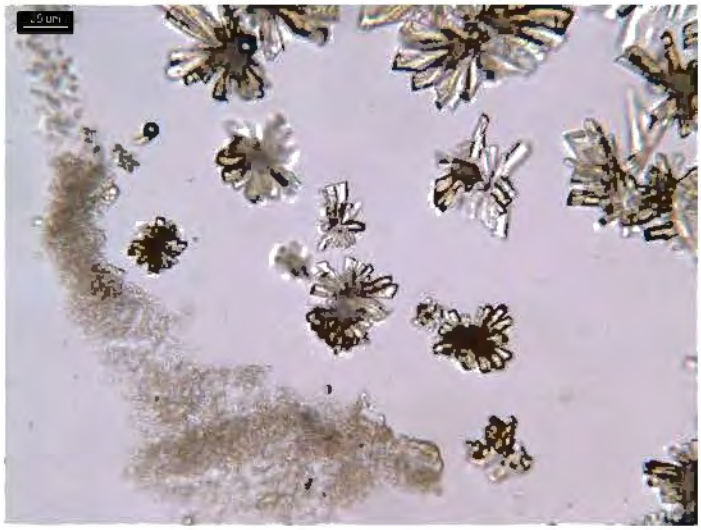


Figure 4. 1 PPP of 4-MEC in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 H_3PO_4 reagent. Crystals form rosettes of rods and blades.

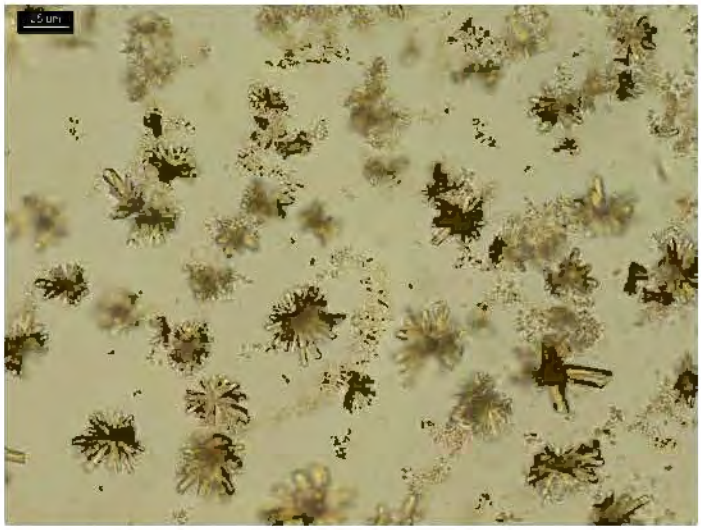


Figure 5. TFMPP:4-MEC mixture (1:1) and 10 µL of H_2PdCl_4 with with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades.

4-MEC: Palladium Chloride with HCl and H_3PO_4 (continued)

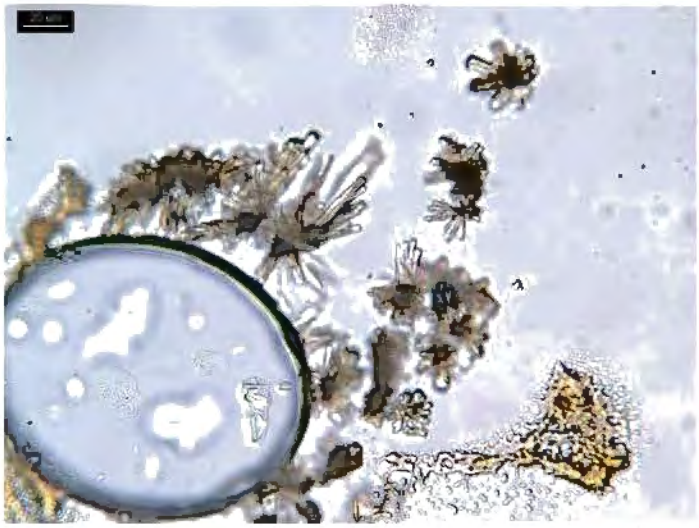


Figure 6. Butylone:4-MEC mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades.

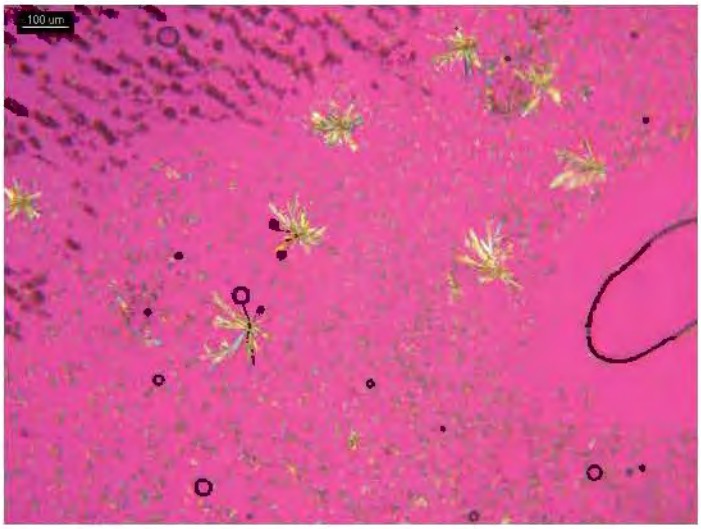


Figure 7. BZP:4-MEC mixture (1:5) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades, sometimes feathery.

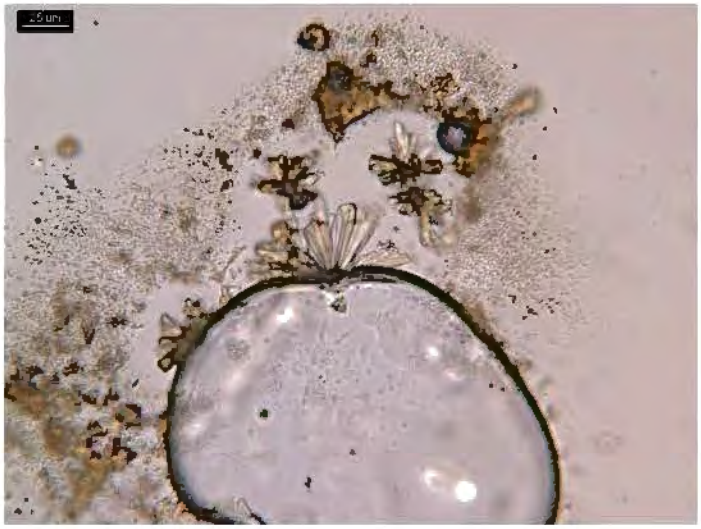


Figure 8. Mephedrone:4-MEC mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades.

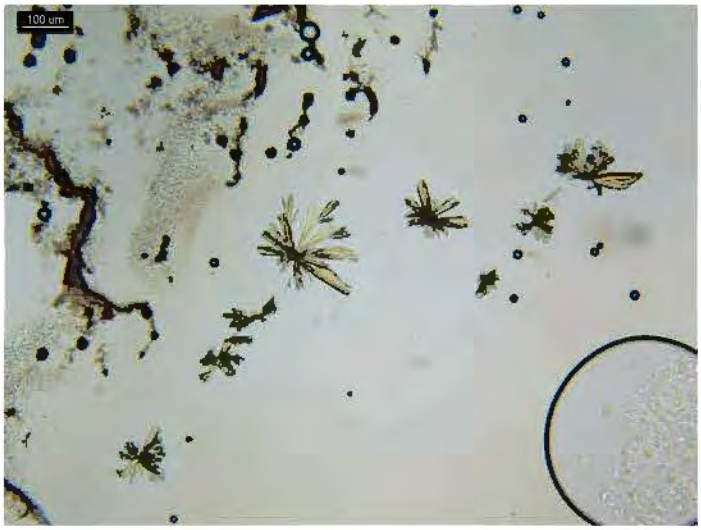


Figure 9. Lidocaine HCl:4-MEC mixture (1:5) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades.

4-MEC: Palladium Chloride with HCl and H_3PO_4 (continued)

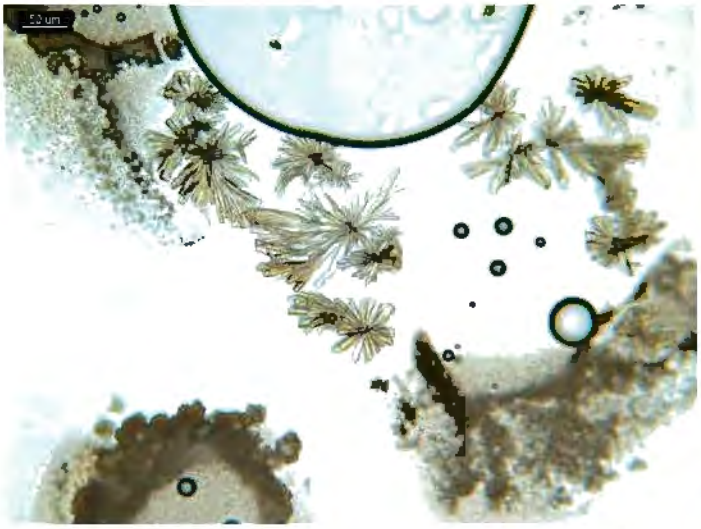


Figure 10. MDPV:4-MEC mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades, sometimes feathery.

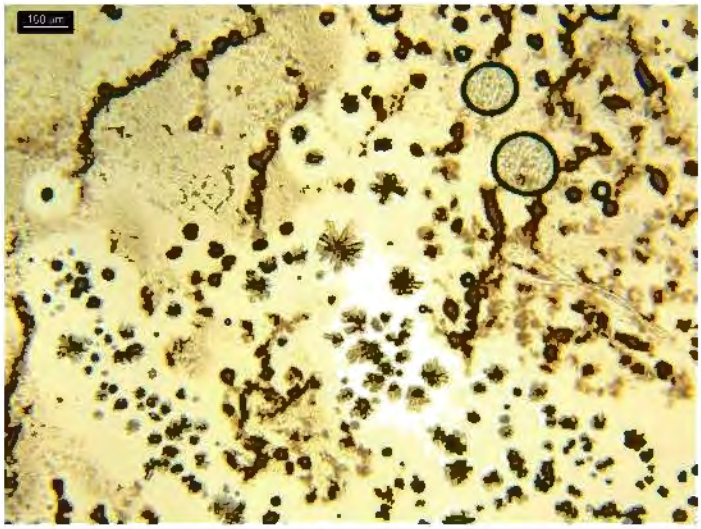


Figure 11. Methylone:4-MEC mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of rods and blades (center).

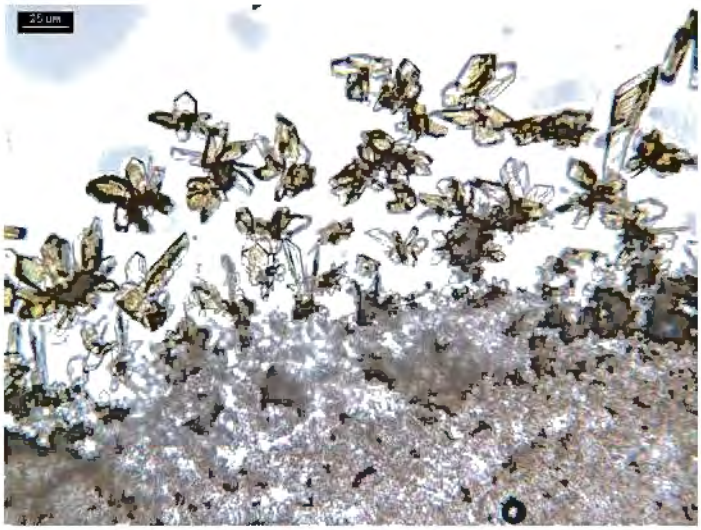


Figure 12. TFMPP forms plates and clusters of plates in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent and no 4-MEC present (negative control test).

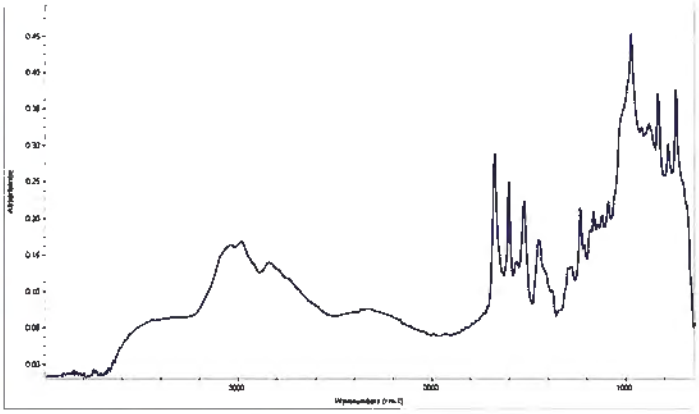


Figure 13. Infrared spectrum of 4-Methylethcathinone (4-MEC) palladium chloride with HCl and H_3PO_4 precipitate. Download/ view SPC file

4-MEC*: Gold Chloride with Sulfuric Acid

REAGENT 2: Gold Chloride ($HAuCl_4$) with Sulfuric Acid ((1+1) H_2SO_4)

$HAuCl_4$ in (1+1) H_2SO_4 is made by combining 1 g of $HAuCl_4 \cdot 3H_2O$ in 20 mL (1+1) H_2SO_4. (1+1) H_2SO_4 is dilute sulfuric acid made by combining one part (e.g. 10 mL) of concentrated sufuric acid with one part (e.g. 10 mL) of water. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈ 5 minutes

Crystal Morphology and Test Notes

Elongated blades and clusters of blades.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of 4-MEC and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent. Crystals form elongated blades and clusters of blades.

Pharmaceuticals, Adulterants, or Other Drug Interactions

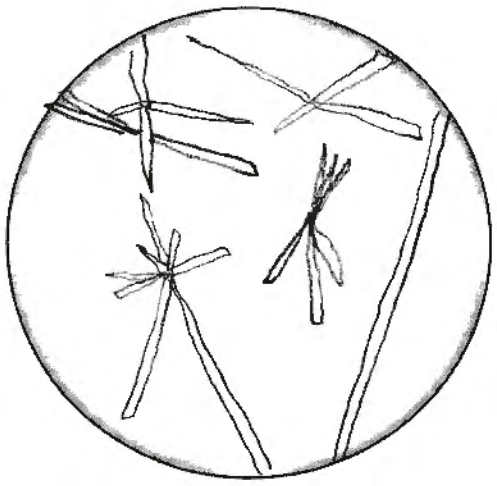
Common adulterants that may inhibit or distort crystal formation include alpha-PVP, butylone, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of 4-MEC with selected adulterants is listed below:

- Aplha-PVP:4-MEC — undetectable at 1:5 and 1:1
- Butylone:4-MEC — detectable at 1:5 and 1:1
- BZP:4-MEC — detectable at 1:5 and 1:1
- Caffeine:4-MEC — detectable at 1:5 and 1:1
- Lidocaine HCl:4-MEC — detectable at 1:5 and 1:1
- MDPV:4-MEC — detectable at 1:5 and 1:1
- Mephedrone:4-MEC — detectable at 1:5 and 1:1
- Methylone:4-MEC — detectable at 1:5 and 1:1
- TFMPP:4-MEC — detectable at 1:5 and 1:1

IR Spectrum

See Figure 7. Download/view SPC file

PLM Optical Properties

Approximate Size Range	Clusters: 100–300 µm Individual blades: 10–30 µm width, 100–400 µm length
Color/Pleochroism	Light yellow; not pleochroic
Refractive Indices (RI)	n-parallel > 1.700 n-perpendicular ≈1.610
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed in water and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique and parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

*4-MEC is another name for 4-Methylethcathinone.

4-MEC: Gold Chloride with Sulfuric Acid (continued)

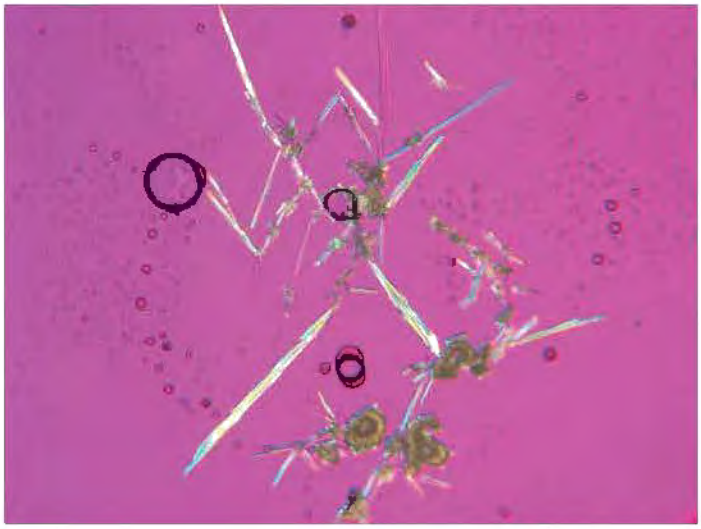


Figure 2. 1 PPP of 4-MEC and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent. Crystals form elongated blades and clusters of blades; crossed polars and Red I compensator.

Figure 3. TFMPP:4-MEC mixture (1:1) and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent; crossed polars and Red I compensator.

Figure 4. Caffeine:4-MEC mixture (1:1) and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent; crossed polars and Red I compensator.

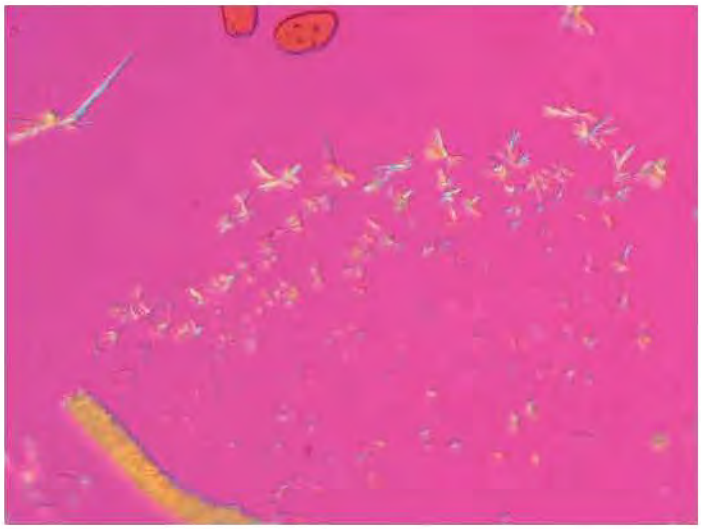


Figure 5. Methylone:4-MEC mixture (1:1) and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent; crossed polars and Red I compensator.

4-MEC: Gold Chloride with Sulfuric Acid (continued)

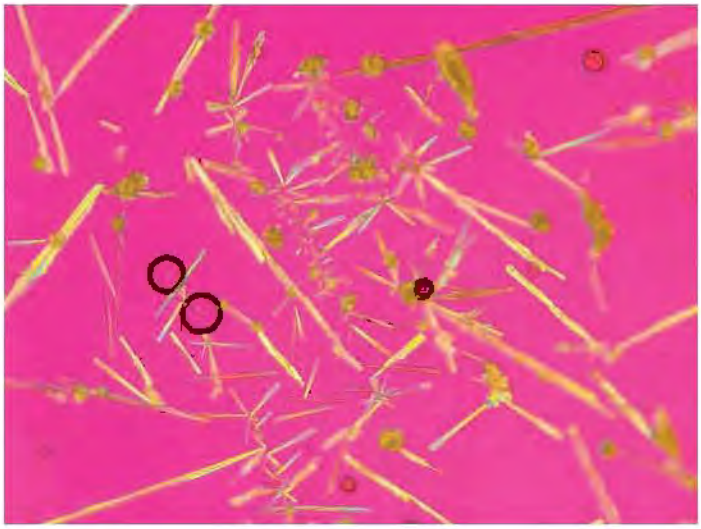


Figure 6. Mephedrone:4-MEC mixture (1:1) and 10 µL of $HAuCl_4$ with (1+1) H_2SO_4 reagent; crossed polars and Red I compensator.

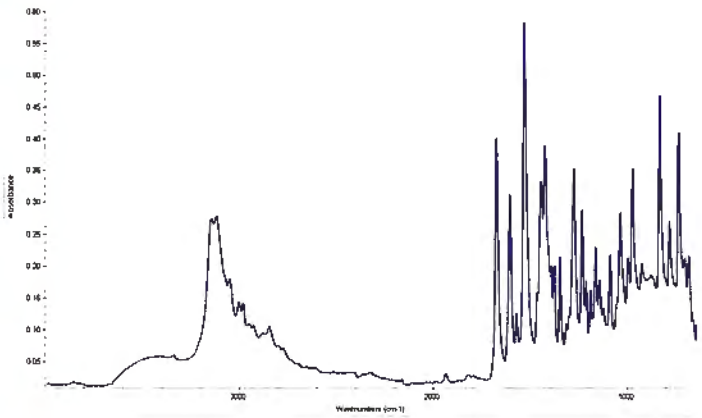


Figure 7. Infrared spectrum of 4-Methylethcathinone (4-MEC) gold chloride with sulfuric acid precipitate. Download/view SPC file

Mephedrone: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample. Or, add reagent directly to sample; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

2–5 minutes

Crystal Morphology and Test Notes

Rosettes and sheaves of rods; sometimes burrs.

Photomicrograph of Typical Crystals

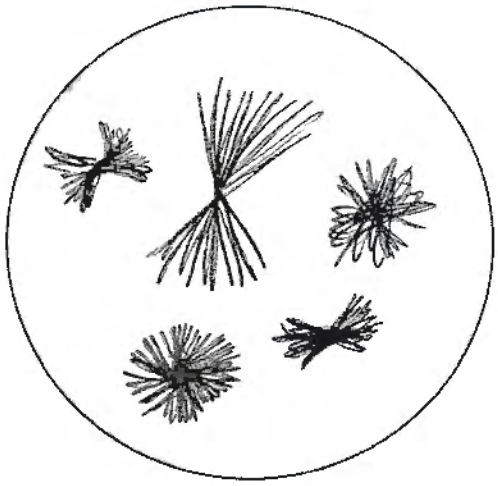
Figure 1. 1 PPP of mephedrone with 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes, sheaves of rods, and sometimes burrs.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, butylone, BZP, caffeine, ethylone, lidocaine HCl, MDPV, methylone, and TFMPP. The detectability of mephedrone with selected adulterants is listed below:

- 4-MEC:mephedrone — detectable at 1:5, 1:1, and 5:1
- Butylone:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1
- BZP:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1
- Caffeine:mephedrone — detectable at 1:5, 1:1, and 5:1
- Ethylone:mephedrone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:mephedrone — detectable at 1:5, 1:1, and 5:1
- MDPV:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1
- Methylone:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1
- TFMPP:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	2.5–5.0 µm width, 25–50 µm length
Color/Pleochroism	Light yellow; not pleochroic
Refractive Indices (RI)	n-parallel < 1.660 n-perpendicular > 1.660
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	Moderate–High
Extinction	Parallel on individual rods
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 11. Download/view SPC file

Mephedrone: Palladium Chloride with HCl and H_3PO_4 (continued)

Figure 2. Same as Figure 1; crossed polars.

Figure 3. Same as Figure 1; crossed polars and Red I compensator.

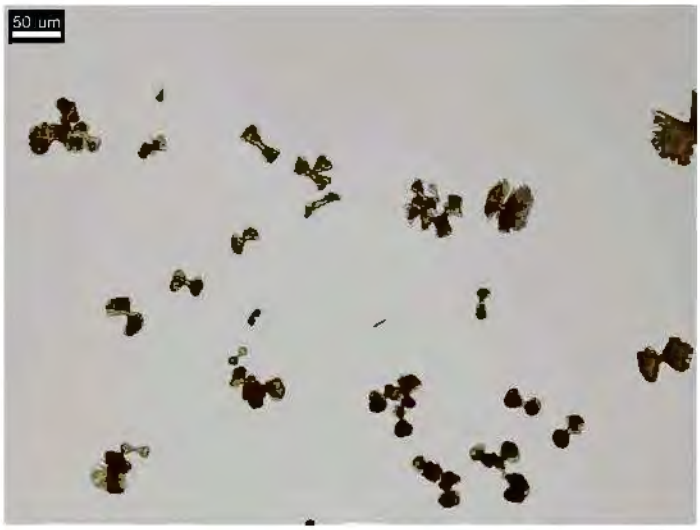


Figure 4. 1 PPP of mephedrone with 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals forms sheaves.

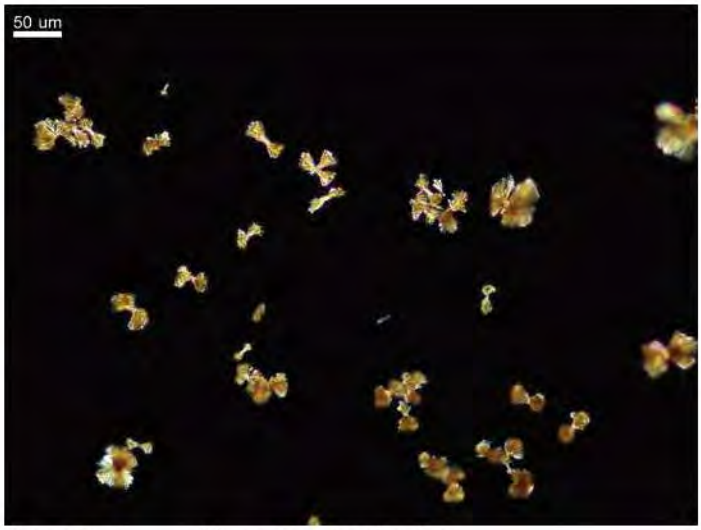


Figure 5. Same as Figure 4; crossed polars.

Figure 7. BZP:mephedrone mixture (1:1) with 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form sheaves.

Mephedrone: Palladium Chloride with HCl and H_3PO_4 (continued)

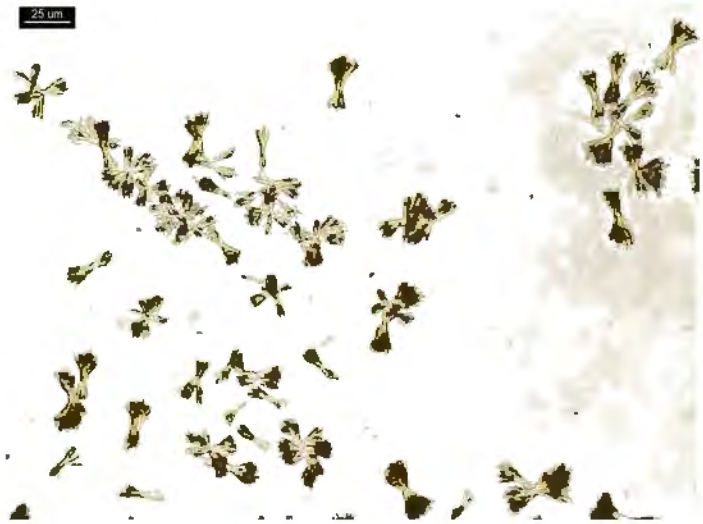


Figure 8. 4-MEC:mephedrone mixture (5:1) with 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form sheaves.

Figure 9. Lidocaine HCl:mephedrone mixture (5:1) with 10 µL of $H_2PdCl_4$with HCl and H_3PO_4 reagent. Crystals form sheaves.

Figure 10. MDPV:mephedrone mixture (1:1) with 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form sheaves.

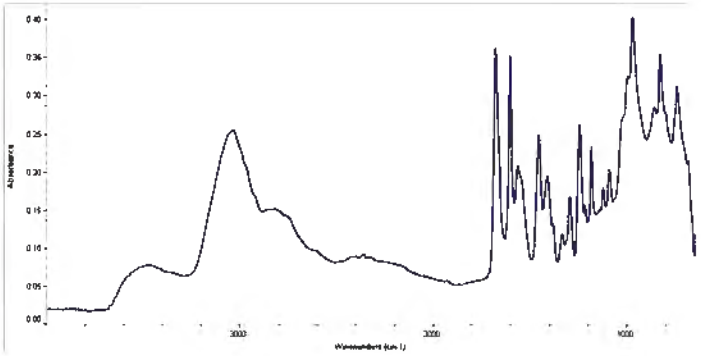


Figure 11. Infrared spectrum of mephedrone palladium chloride with HCl and H_3PO_4 precipitate. Download/view SPC file

Mephedrone: Picrolonic Acid

REAGENT 2: Picrolonic Acid ($C_{10}H_8N_4O_5$)

Saturated aqueous: 25 mg of picrolonic acid in H_2O, make up to 10 mL.

Test Method

Direct test: Place a 5–10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample. Or, add reagent directly to sample; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Dendrites and rosettes of dendrites.

Photomicrograph of Typical Crystals

Figure 1. 2 PPP of mephedrone in 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

Pharmaceuticals, Adulterants, or Other Drug Interactions

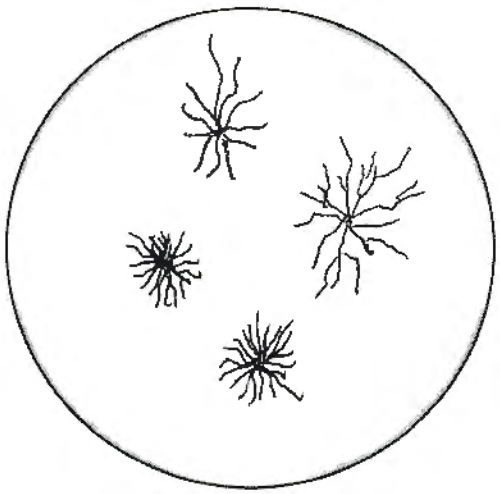
Common adulterants that may inhibit or distort crystal formation include 4-MEC, butylone, BZP, caffeine, ethylone, lidocaine HCl, MDPV, methylone, and TFMPP. The detectability of mephedrone with selected adulterants is listed below:

- 4-MEC:mephedrone — detectable at 1:5, 1:1, and 5:1
- Butylone:mephedrone — detectable at 1:5, 1:1, and 5:1
- BZP:mephedrone — detectable at 1:5, 1:1, and 5:1
- Caffeine:mephedrone — detectable at 1:5 and 1:1; undetectable at 5:1
- Ethylone:mephedrone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:mephedrone — detectable at 1:5, 1:1, and 5:1
- MDPV:mephedrone — detectable at 1:5, 1:1, and 5:1
- Methylone:mephedrone — detectable at 1:5, 1:1, and 5:1
- TFMPP:mephedrone — detectable at 1:5, 1:1, and 5:1

IR Spectrum

See Figure 10. Download/view SPC file

PLM Optical Properties

Approximate Size Range	2–5 µm width; length can be up to 500 µm
Color/Pleochroism	Colorless to pale yellow; not pleochroic
Refractive Indices (RI)	n-parallel ≈ 1.500 n-perpendicular ≈ 1.560
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Room temperature
Estimated Birefringence	High
Extinction	Dendrite branches: complete, parallel and oblique
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Mephedrone: Picrolonic Acid (continued)

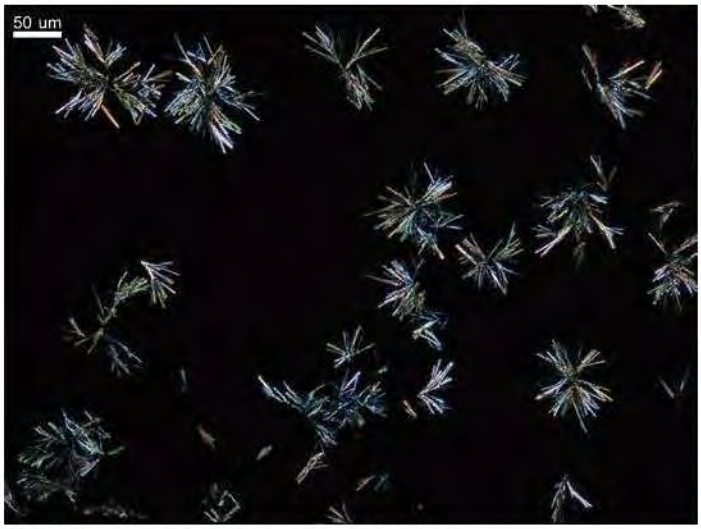


Figure 2. Same as Figure 1; crossed polars.

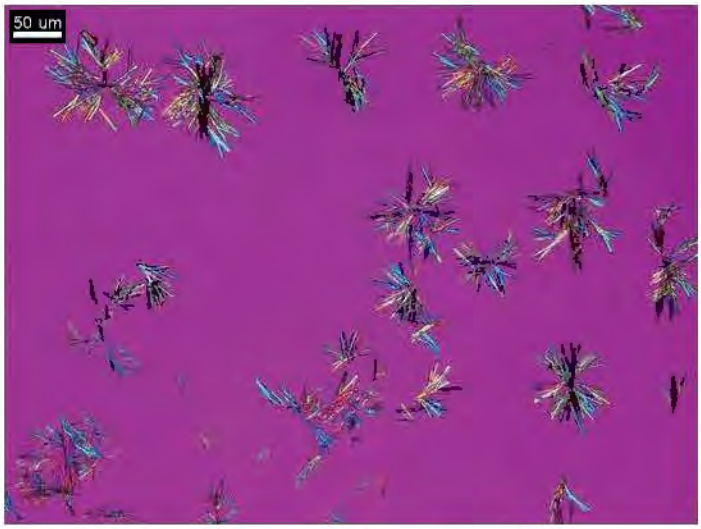


Figure 3. Same as Figure 1; crossed polars and Red I compensator.

Figure 4. BZP:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

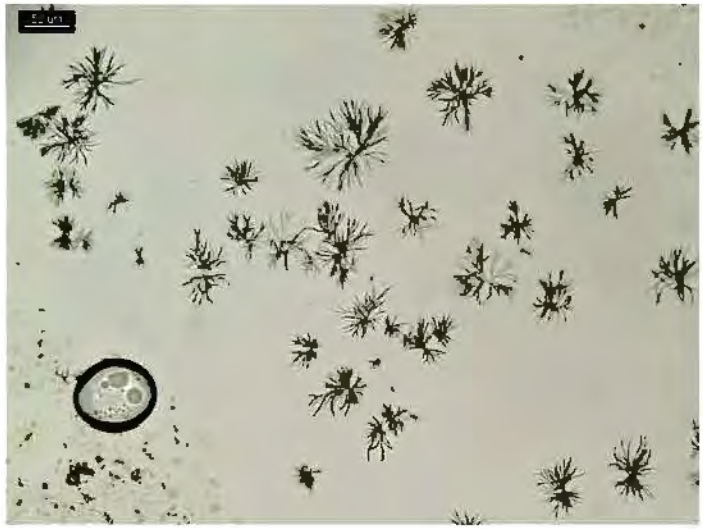


Figure 5. Butylone:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

Mephedrone: Picrolonic Acid (continued)

Figure 6. Lidocaine HCl:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

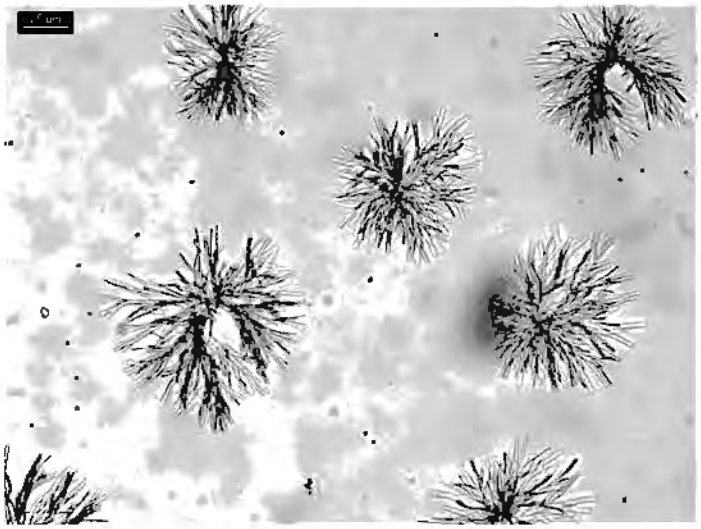


Figure 7. MDPV:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form rosettes of dendrites.

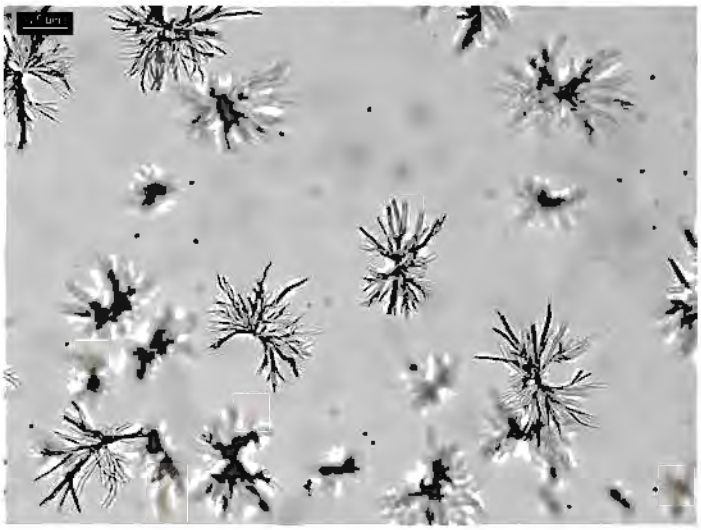


Figure 8. Ethylone:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

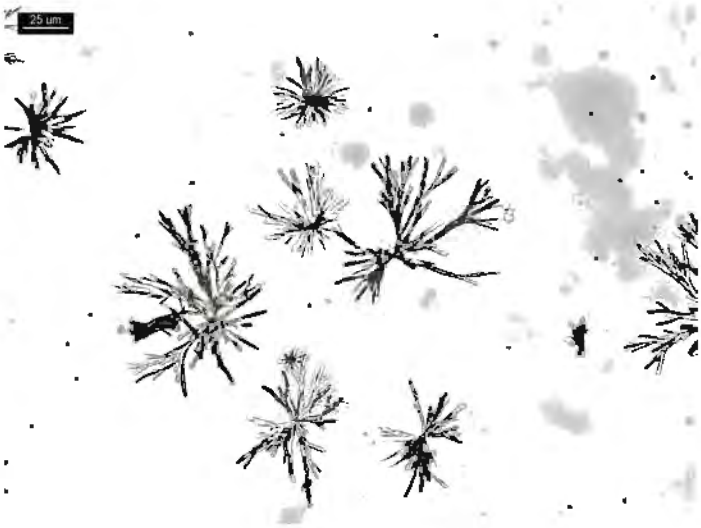


Figure 9. Methylone:mephedrone mixture (5:1) with 10 µL of $C_{10}H_8N_4O_5$ reagent. Crystals form dendrites and rosettes of dendrites.

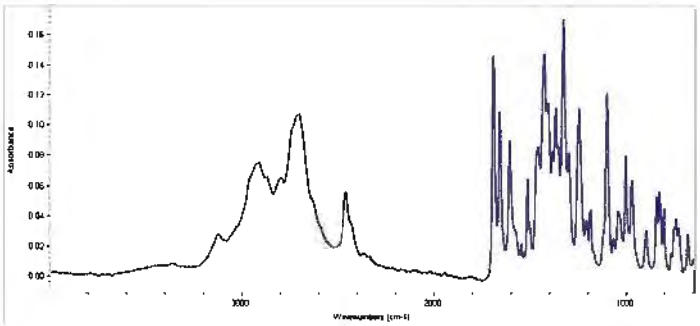


Figure 10. Infrared spectrum of mephedrone picrolonic acid precipitate. Download/view SPC file

Methylone: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample. Or, add reagent directly to sample; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈1 minute (adulterants up to ≈15 minutes)

Crystal Morphology and Test Notes

Rosettes of plates (colorless). Crystals also form sheaves after 15 minutes.

Photomicrograph of Typical Crystals

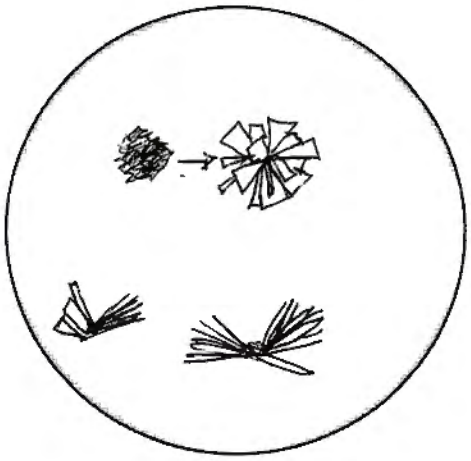
Figure 1. 1 PPP of methylone in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of plates.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, butylone, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, and TFMPP. The detectability of methylone with selected adulterants is listed below:

- 4-MEC:methylone — detectable at 1:5, 1:1, and 5:1
- Alpha-PVP:methylone — detectable at 1:5, 1:1, and 5:1
- Butylone:methylone — detectable at 1:5, 1:1, and 5:1
- BZP:methylone — detectable at 1:5 and 1:1; undetectable at 5:1
- Caffeine:methylone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:methylone — detectable at 1:5, 1:1, and 5:1
- MDPV:methylone — detectable at 1:5, 1:1, and 5:1
- Mephedrone:methylone — detectable at 1:5, 1:1, and 5:1
- TFMPP:methylone — detectable at 1:5, 1:1, and 5:1

PLM Optical Properties

Approximate Size Range	Rosettes: 5–100 µm Sheaves: 50–125 µm length, 10–50 µm width
Color/Pleochroism	Rosettes of plates: Colorless to brown, not pleochroic. Sheaves: Pleochroic, red-orange (perpendicular) to brown (parallel).
Refractive Indices (RI)	n_1 ≈1.700 and >1.700 n_2 ≈1.590 (rosettes of plates) and 1.550 (sheaves)
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Oblique
Sign of Elongation	Rosettes of plates: Positive (+) and negative (–) Sheaves: Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Methylone: Palladium Chloride with HCl and H_3PO_4 (continued)

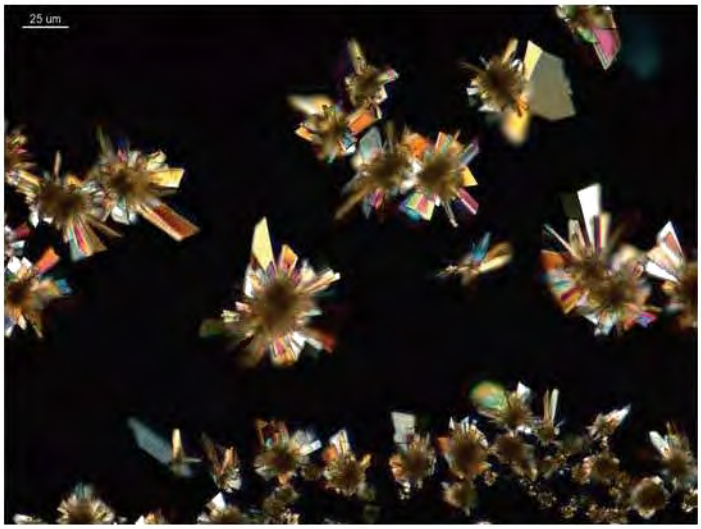


Figure 2. Same as Figure 1; crossed polars.

Figure 3. Same as Figure 1; crossed polars and Red I compensator.

Figure 4. 1 PPP of methylone in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form sheaves after 15 minutes.

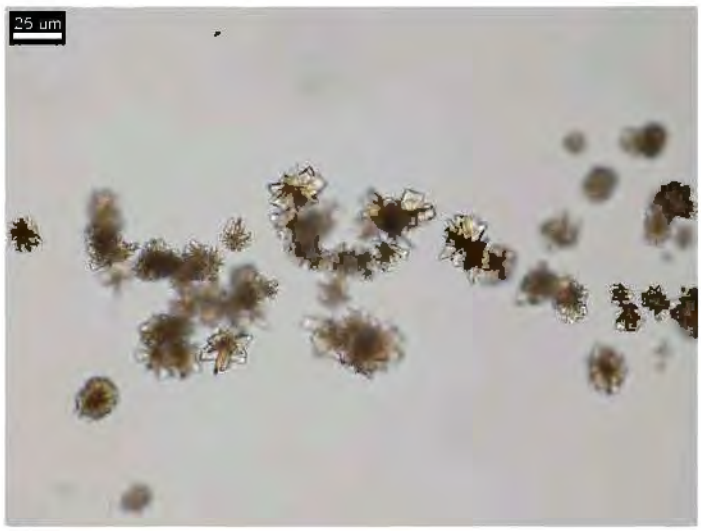


Figure 5. Alpha-PVP:methylone mixture (1:1) in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of plates.

Methylone: Palladium Chloride with HCl and H_3PO_4 (continued)

Figure 6. Caffeine:methylone mixture (1:1) in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of plates.

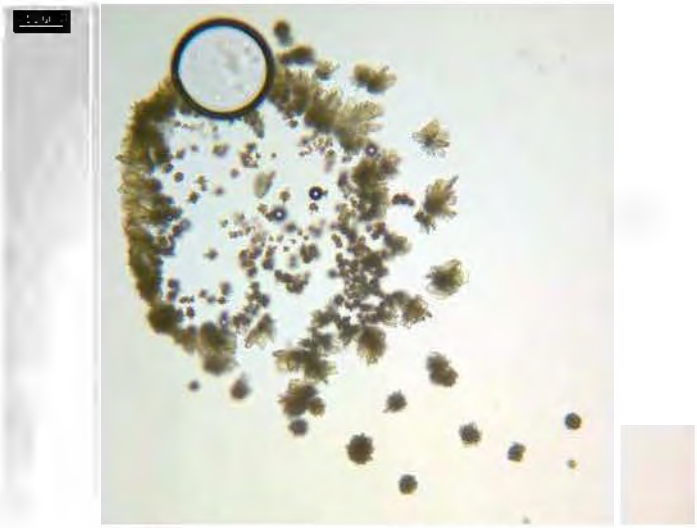


Figure 7. Mephedrone:methylone mixture (5:1) in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form rosettes of plates.

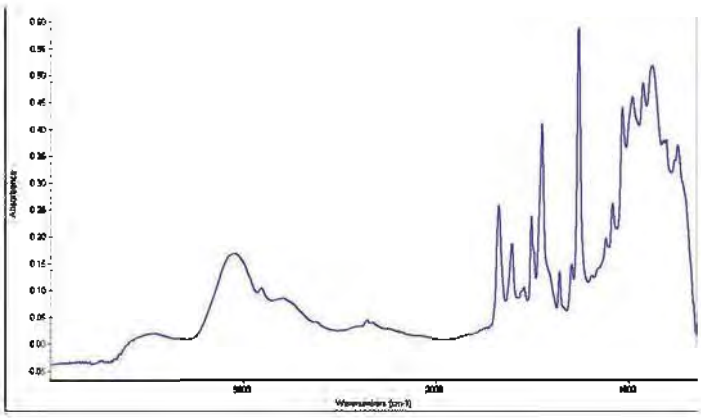


Figure 8. Infrared spectrum of methylone palladium chloride with HCl and H_3PO_4 precipitate. Download/view SPC file

Methylone: Picric Acid

REAGENT 2: Picric Acid ($C_6H_2(NO_2)_3OH$)

Picric acid, saturated aqueous solution

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediately

Crystal Morphology and Test Notes

Burrs and rosettes of needles

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of methylone and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

Pharmaceuticals, Adulterants, or Other Drug Interactions

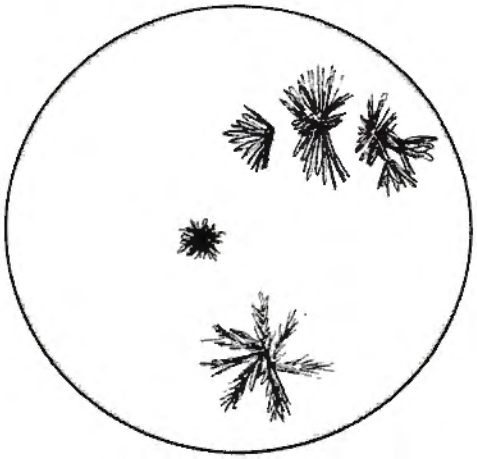
Common adulterants that may inhibit or distort crystal formation include 4-MEC, alpha-PVP, butylone, BZP, caffeine, lidocaine HCl, MDPV, mephedrone, and TFMPP. The detectability of methylone with selected adulterants is listed below:

- 4-MEC:methylone — detectable at 1:5, 1:1, and 5:1
- Alpha-PVP:methylone — detectable at 1:5, 1:1, and 5:1
- Butylone:methylone — detectable at 1:5, 1:1, and 5:1
- BZP:methylone — detectable at 1:5, 1:1, and 5:1
- Caffeine:methylone — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:methylone — detectable at 1:5 and 1:1; undetectable at 5:1
- MDPV:methylone — detectable at 1:5; undetectable at 1:1, and 5:1
- Mephedrone:methylone — detectable at 1:5, 1:1, and 5:1
- TFMPP:methylone — detectable at 1:5, 1:1, and 5:1

IR Spectrum

See Figure 10. Download/view SPC file

PLM Optical Properties

Approximate Size Range	10–100 µm
Color/Pleochroism	Yellow. Pleochoric: pale yellow (parallel) to yellow (perpendicular)
Refractive Indices (RI)	n-parallel ≈1.520 n-perpendicular ≈1.620
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed in absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Parallel and oblique (individual needles)
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Methylone: Picric Acid (continued)

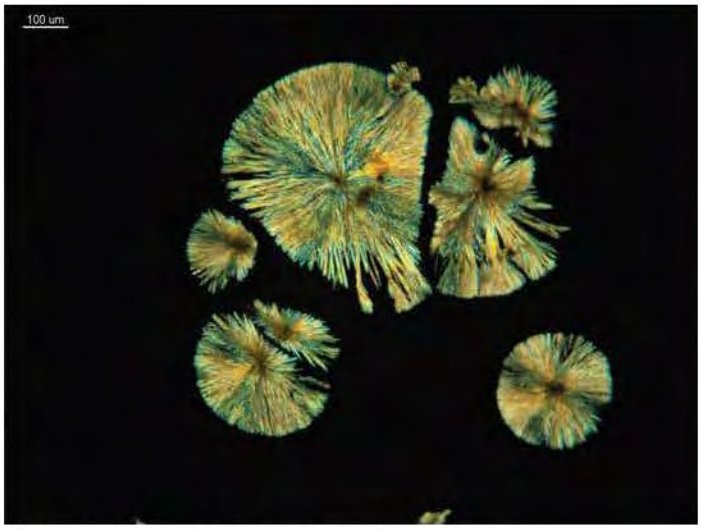


Figure 2. Same as Figure 1; crossed polars.

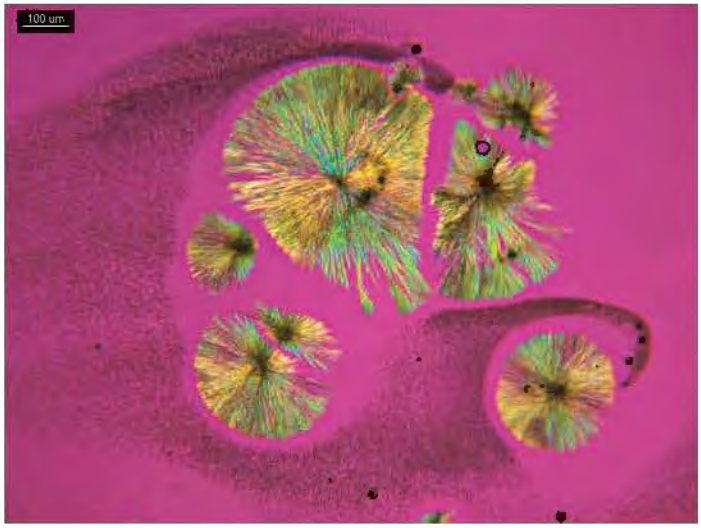


Figure 3. Same as Figure 1; crossed polars and Red I compensator.

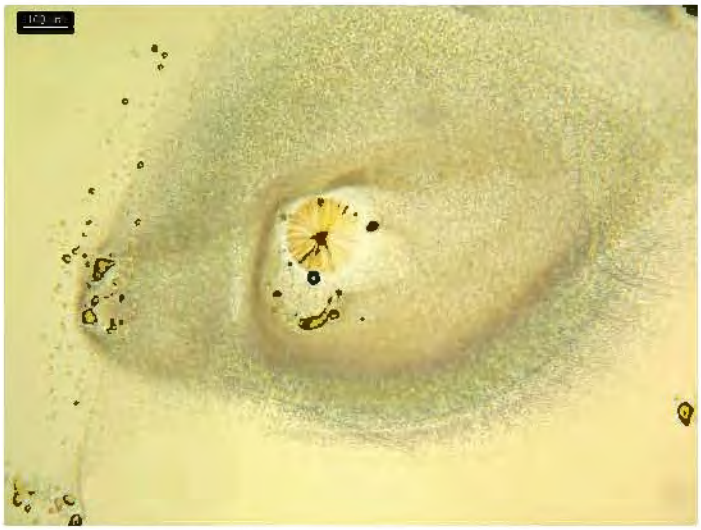


Figure 4. Lidocaine HCl:methylone mixture (1:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

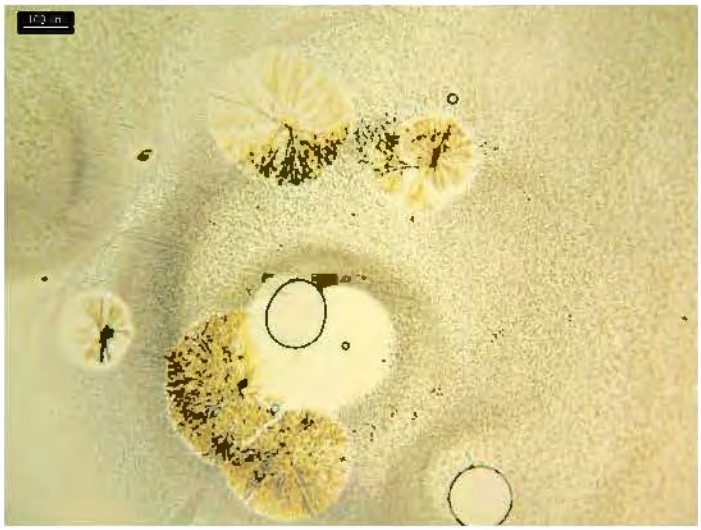


Figure 5. Mephedrone:methylone mixture (5:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

Methylone: Picric Acid (continued)

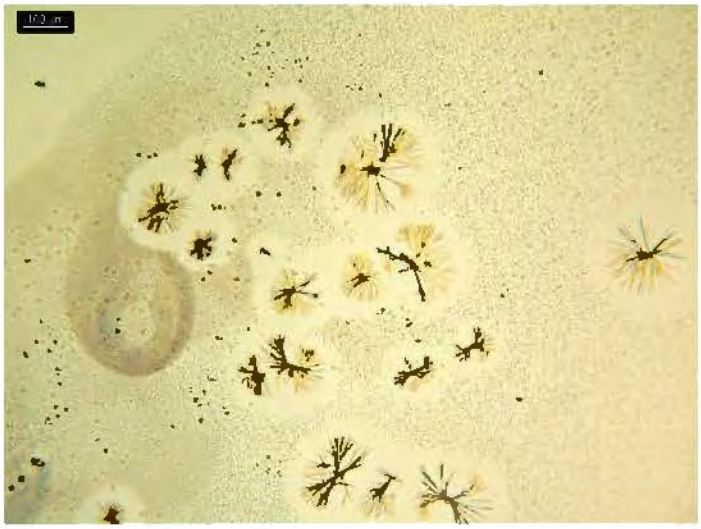


Figure 6. 4-MEC:methylone mixture (5:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

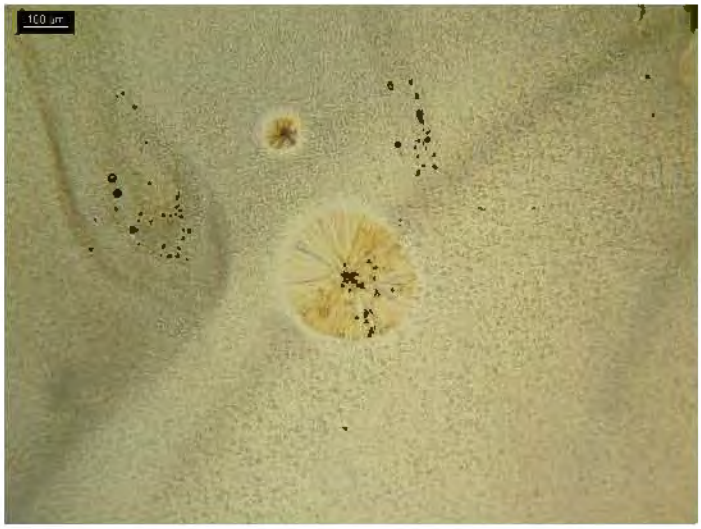


Figure 7. Alpha-PVP:methylone mixture (5:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

Figure 8. Butylone:methylone mixture (5:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

Figure 9. Caffeine:methylone mixture (5:1) and 10 µL of picric acid reagent. Crystals form burrs and rosettes of needles.

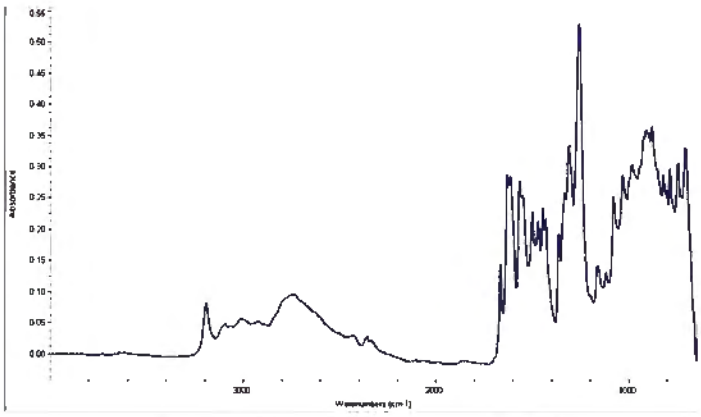


Figure 10. Infrared spectrum of methylone picric acid precipitate. Download/view SPC file

Alpha-PVP*: Palladium Chloride with HCl and H_3PO_4

REAGENT 1: Palladium Chloride (H_2PdCl_4) with Concentrated Hydrochloric Acid (HCl) and Concentrated Phosphoric Acid (H_3PO_4)

H_2PdCl_4 in concentrated H_3PO_4 is made by combining 1 g of $PdCl_2$ with 0.9 mL of concentrated HCl, then make up to 20 mL with concentrated H_3PO_4.

Test Method

Direct test: Place a 10 µL drop of reagent on a coverslip. Invert coverslip and place it directly onto the sample.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

5–6 minutes

Crystal Morphology and Test Notes

Clusters of elongated blades, sometimes sheaves. Crystals resembling corn stalks and bouquets of flowers are also visible.

Photomicrograph of Typical Crystals

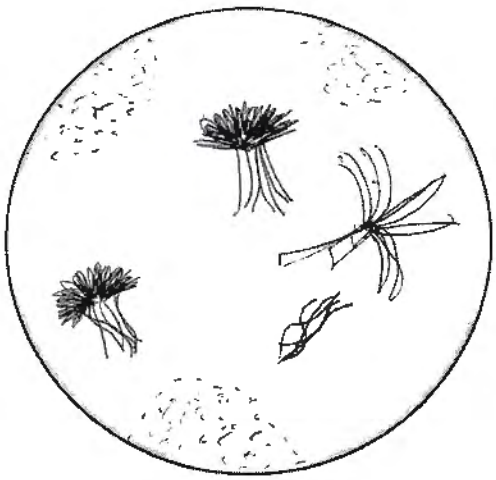
Figure 1. 1 PPP of alpha-PVP in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form clusters of elongated blades, sheaves, bouquets of flowers, and corn stalks.

Pharmaceuticals, Adulterants, or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, butylone, BZP, caffeine, ethylone, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of alpha-PVP with selected adulterants is listed below:

- 4-MEC:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- Butylone:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- BZP:alpha-PVP— detectable at 1:5, 1:1; undetectable at 5:1
- Caffeine:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- Ethylone:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- Lidocaine HCl:alpha-PVP — detectable at 1:5, 1:1; undetectable at 5:1
- MDPV:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- Mephedrone:alpha-PVP — detectable at 1:5, 1:1; undetectable at 5:1
- Methylone:alpha-PVP — detectable at 1:5, 1:1, and 5:1
- TFMPP:alpha-PVP — detectable at 1:5, 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	Sheaves: 20–150 µm Individual blades: 25–45 µm length
Color/Pleochroism	Yellow. Pleochroic: light yellow (parallel) to yellow (perpendicular)
Refractive Indices (RI)	≈1.590 >1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked with lab tissue then washed in absolute ethanol and dried at room temperature.
Estimated Birefringence	High
Extinction	Parallel and oblique (individual blades)
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

*Alpha-PVP is another name for α-Pyrrolidinopentiophenone or α-Pyrrolidinovalerophenone.

Alpha-PVP: Palladium Chloride with HCl and H_3PO_4 (continued)

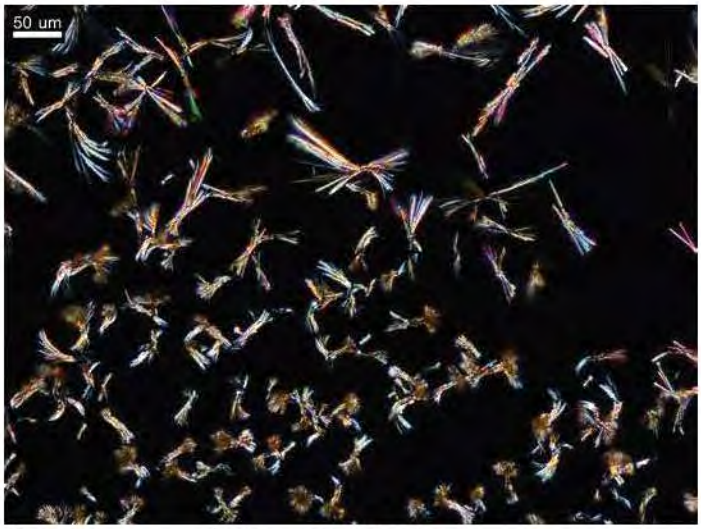


Figure 2. Same as Figure 1; crossed polars.

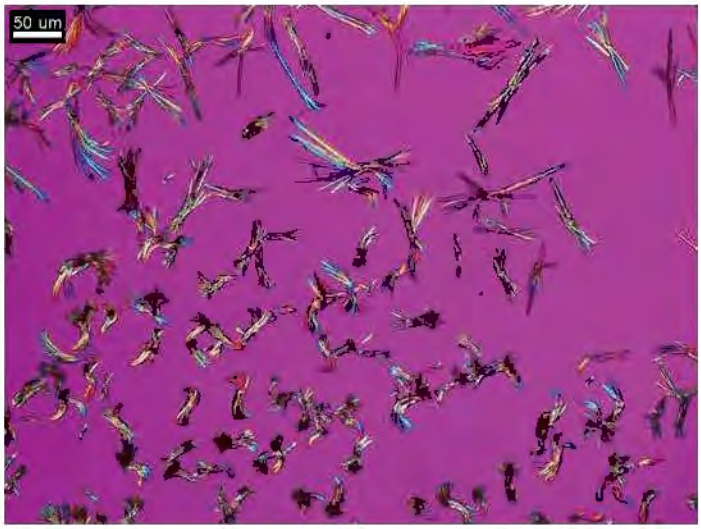


Figure 3. Same as Figure 1; crossed polars and Red I compensator.

Figure 4. 1 PPP of alpha-PVP in 10 µL of H_2PdCl_4 with HCl and H_3PO_4reagent. Crystals form clusters of elongated blades, sheaves, bouquets of flowers, and corn stalks.

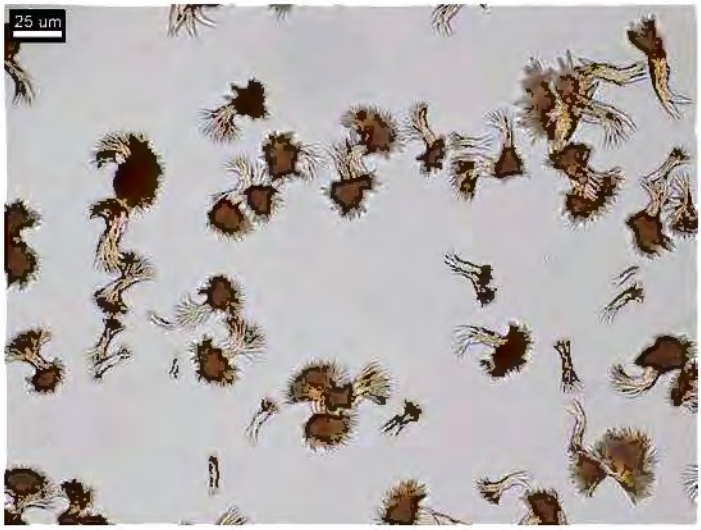


Figure 5. 1 PPP of alpha-PVP in 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form sheaves, bouquets of flowers, and corn stalks.

Alpha-PVP: Palladium Chloride with HCl and H_3PO_4 (continued)

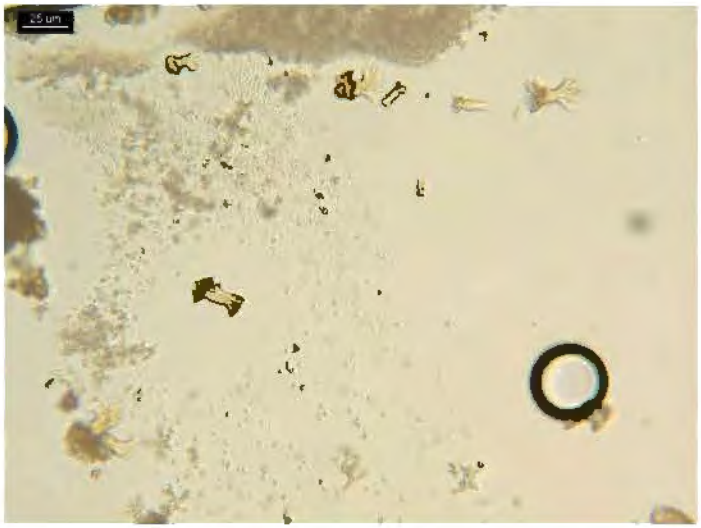


Figure 6. Ethylone:alpha-PVP mixture (5:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form bouquets of flowers.

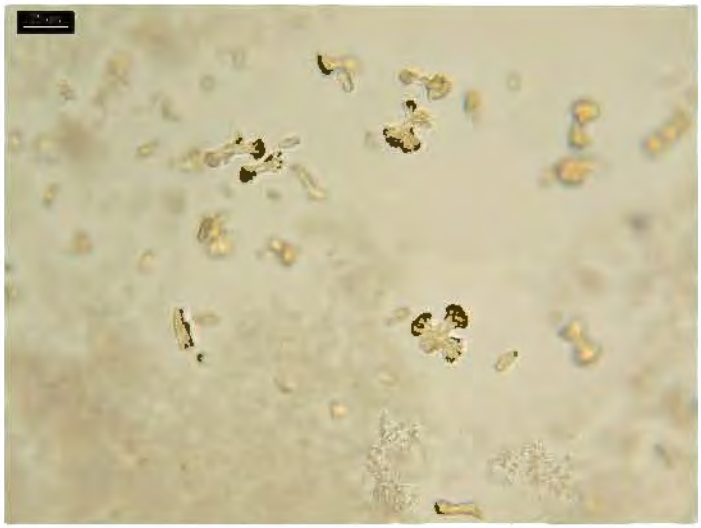


Figure 7. Lidocaine HCl:alpha-PVP mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form bouquets of flowers.

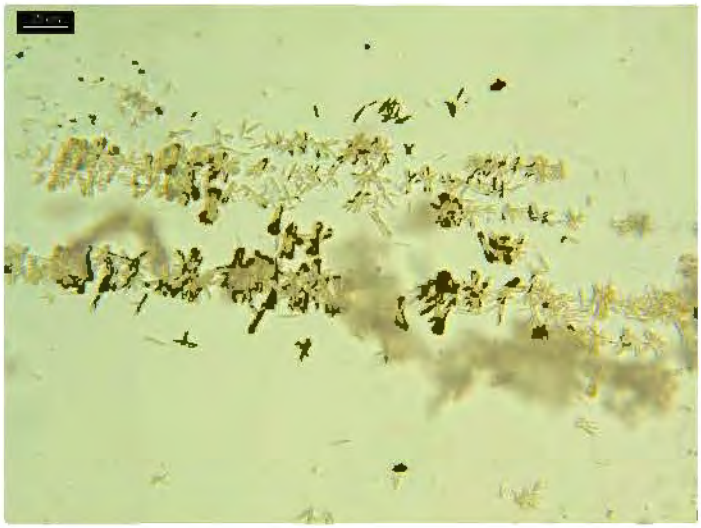


Figure 8. Mephedrone:alpha-PVP mixture (1:1) and 10 µL of H_2PdCl_4 with HCl and H_3PO_4 reagent. Crystals form clusters of elongated blades, sheaves, bouquets of flowers, and corn stalks.

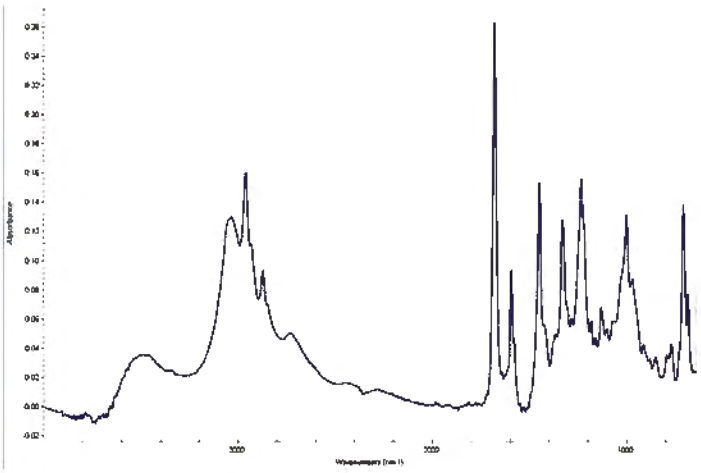


Figure 9. Infrared spectrum of alpha-PVP palladium chloride with HCl and H_3PO_4 precipitate. Download/view SPC file

Alpha-PVP*: Potassium Ferrocyanide with Hydrochloric Acid

REAGENT 2: Potassium Ferrocyanide ($K_4Fe(CN)_6$) with 5% Hydrochloric Acid (HCl)

10% aqueous: 1 g of $K_4Fe(CN)_6 \cdot 3H_2O$ in H_2O, make up to 10 mL. Reagent does not keep; it is colorless and should be used fresh before it gradually turns yellow.

Test Method

Direct test: Dissolve sample in 5 µL of 5% HCl. Add 5 µL of the reagent; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Instant

Crystal Morphology and Test Notes

Crosses and four-pointed stars.

Photomicrograph of Typical Crystals

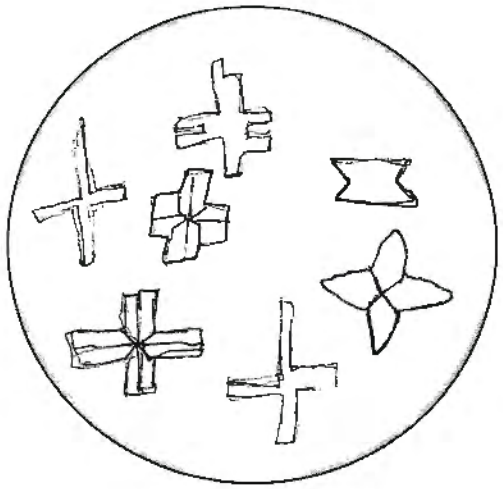
Figure 1. 1 PPP of alpha-PVP in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form four-pointed stars.

Pharmaceuticals, Adulterants or Other Drug Interactions

Common adulterants that may inhibit or distort crystal formation include 4-MEC, butylone, BZP, caffeine, ethylone, lidocaine HCl, MDPV, mephedrone, methylone, and TFMPP. The detectability of alpha-PVP with selected adulterants is listed below:

- 4-MEC:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1
- Butylone:alpha-PVP — detectable at at 1:5, 1:1, and 5:1
- BZP:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1
- Caffeine:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1
- Ethylone:alpha-PVP — detectable at at 1:5, 1:1, and 5:1
- Lidocaine HCl:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1
- MDPV:alpha-PVP — detectable at at 1:5, 1:1, and 5:1
- Mephedrone:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1
- Methylone:alpha-PVP — detectable at at 1:5, 1:1, and 5:1
- TFMPP:alpha-PVP — detectable at 1:5 and 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	2.5–20 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	Indeterminable; crystals did not dry or were obscured by recrystallization of the reagent.
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Not applicable
Estimated Birefringence	Moderate–High
Extinction	Incomplete
Sign of Elongation	Positive (+) on four-pointed stars Negative (–) on elongated crosses
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

*Alpha-PVP is another name for α-Pyrrolidinopentiophenone or α-Pyrrolidinovalerophenone.

Alpha-PVP: Potassium Ferrocyanide with Hydrochloric Acid (continued)

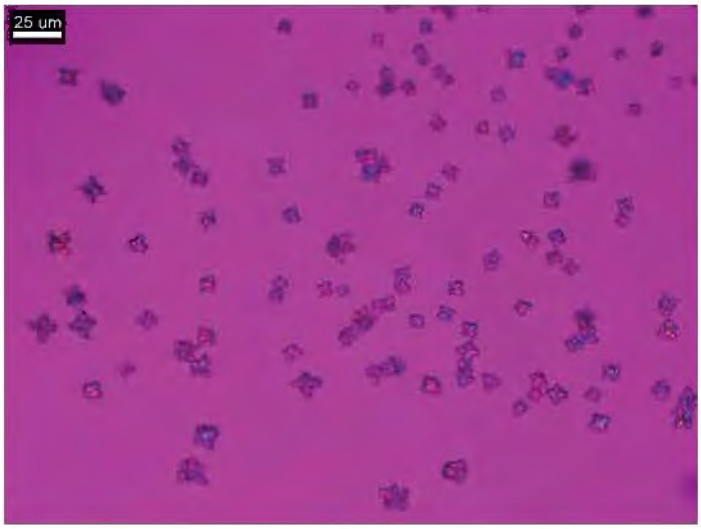


Figure 2. Same as Figure 1; crossed polars and Red I compensator.

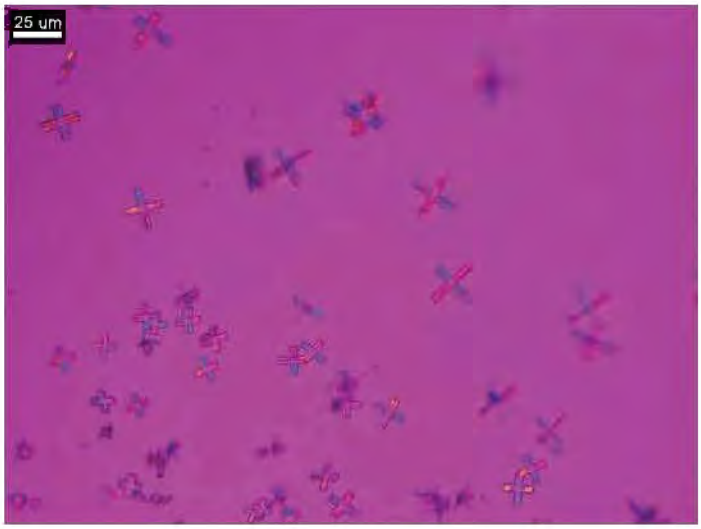


Figure 3. 1 PPP of alpha-PVP in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form crosses; crossed polars and Red I compensator.

Figure 4. 1 PPP of alpha-PVP in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form four-pointed stars; crossed polars and Red I compensator.

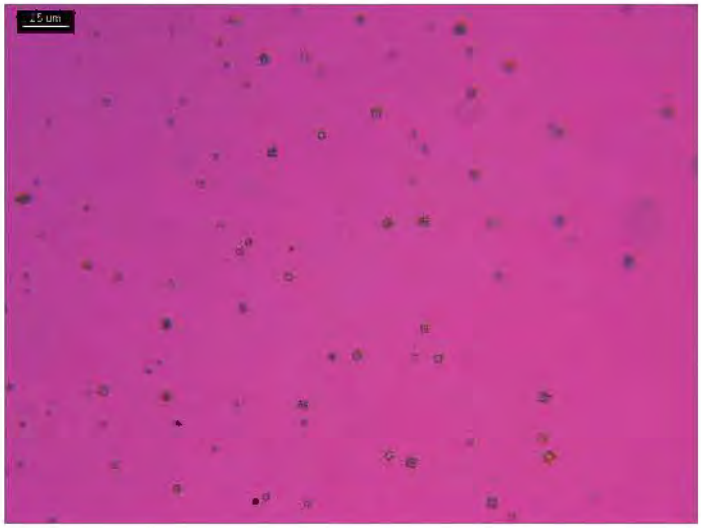


Figure 5. Methylone:alpha-PVP mixture (5:1) in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form four-pointed stars; crossed polars and Red I compensator.

Alpha-PVP: Potassium Ferrocyanide with Hydrochloric Acid (continued)

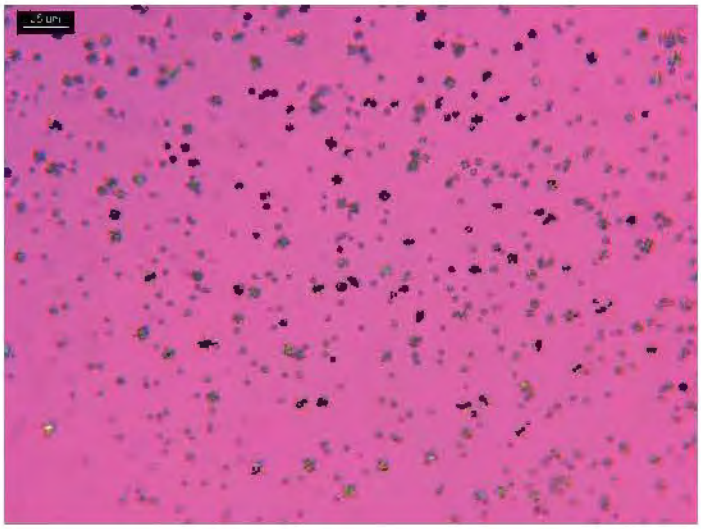


Figure 6. Licocaine HCl:alpha-PVP mixture (1:1) in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form four-pointed stars and crosses; crossed polars and Red I compensator.

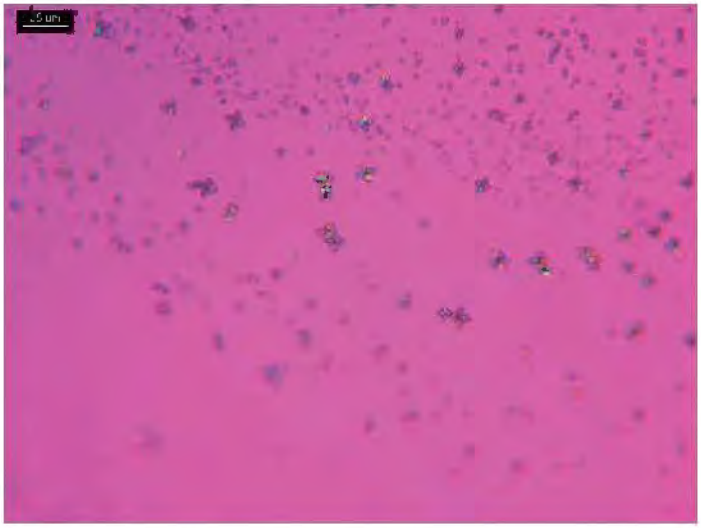


Figure 7. 4-MEC:alpha-PVP mixture (1:1) in 5 µL of 5% HCl and 5 µL of $K_4Fe(CN)_6$ reagent; no coverslip. Crystals form four-pointed stars; crossed polars and Red I compensator.

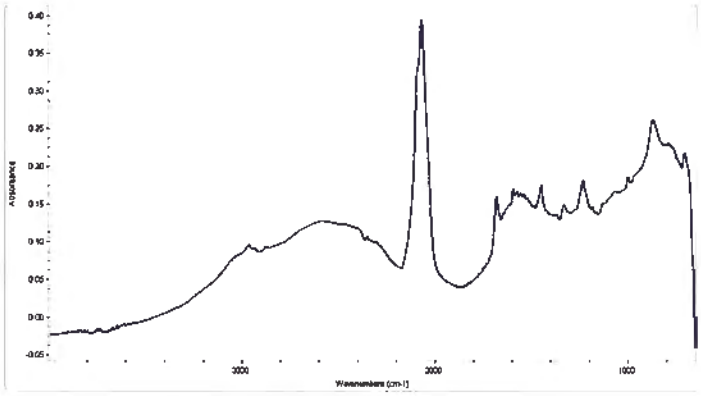


Figure 9. Infrared spectrum of alpha-PVP potassium ferrocyanide and 5% hydrochloric acid precipitate. Download/ view SPC file

Tramadol: Gold Bromide with HOAc and H_2SO_4

REAGENT 1A: Gold Bromide ($HAuBr_4$) with Acetic Acid (HOAc) and Sulfuric Acid ((2+3) H_2SO_4)

There are two ways to make this reagent: 1.3 g $HAuBr_4$ in (2+3) H_2SO_4, make up to 30 mL. (2+3) H_2SO_4 is dilute sulfuric acid made by combining two parts (e.g. 12 mL) of concentrated sulfuric acid with three parts (e.g. 18 mL) of water. Then add 10 mL of glacial HOAc. Alternatively, to convert gold chloride to gold bromide: 1 g $HAuCl_4 \cdot 3H_2O$ and 1.5 mL HBr (40%) in (2+3) H_2SO_4, make up to 30 mL. Then add 10 mL of glacial HOAc.

Test Method

Direct test: Dissolve sample in 2 µL of H_2O, then add a 10 µL reagent drop on a coverslip, invert the coverslip and place it directly onto the sample, or add 10 µL of reagent directly to the sample on a glass slide.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈2 minutes

Crystal Morphology and Test Notes

Parallelograms, rectangular plates, some bow ties and X-shaped crystals.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of tramadol in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form parallelograms, rectangular plates, bow ties, and X-shaped crystals.

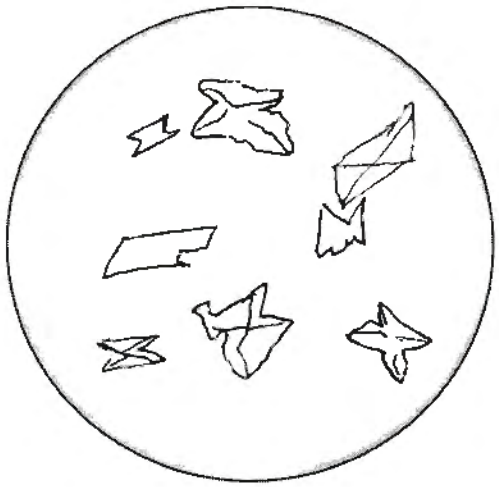
Pharmaceuticals, Adulterants, or Other Drug Interactions

This test was successful on pharmaceutical tablets from two manufacturers (Apotex® and Kali®), each containing 37.5 mg of tramadol and 325 mg of acetaminophen using 2 PPPs. It was also successful on tablets from two other manufacturers (McNeil®and Mylan®), each containing 50 mg of tramadol using 1 PPP, and on a tablet (Patriot®) containing 100 mg of tramadol using 1 PPP; no extraction procedures were necessary.

IR Spectrum

See Figure 9. Download/view SPC file

PLM Optical Properties

Approximate Size Range	5–200 µm
Color/Pleochroism	Orange-yellow. Pleochroic: yellow to orange
Refractive Indices (RI)	n > 1.700. Crystals are soluble in 1.700 RI liquid.
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with water and xylene and dried at room temperature.
Estimated Birefringence	High
Extinction	Parallel and oblique
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Biaxial (optic sign indeterminable)

Tramadol: Gold Bromide with HOAc and H_2SO_4 (continued)

Figure 2. 1 PPP of tramadol in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form parallelograms, rectangular plates, bow ties, and X-shaped crystals.

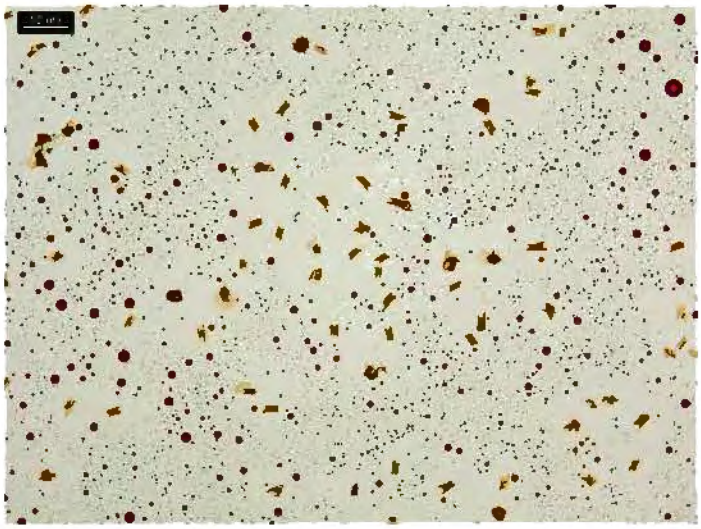


Figure 3. 1 PPP of tramadol in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form parallelograms and rectangular plates.

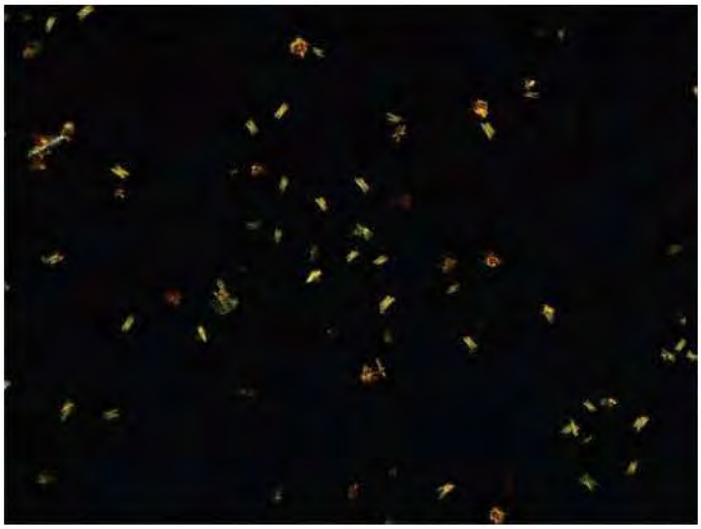


Figure 4. Same as Figure 3; crossed polars.

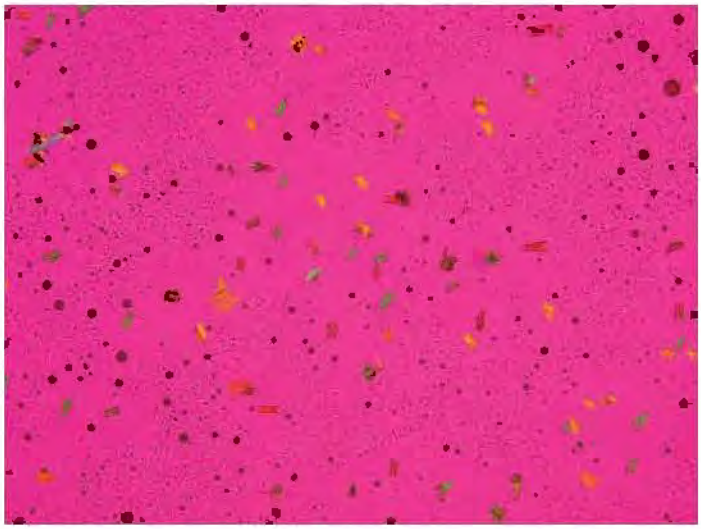


Figure 5. Same as Figure 3; crossed polars and Red I compensator.

Tramadol: Gold Bromide with HOAc and H_2SO_4 (continued)

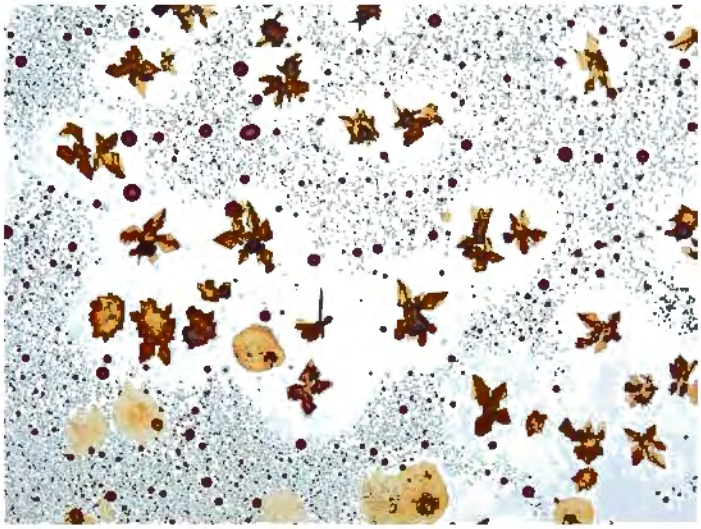


Figure 6. 1 PPP from a 100 mg tramadol tablet in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form bow ties and X-shaped crystals.

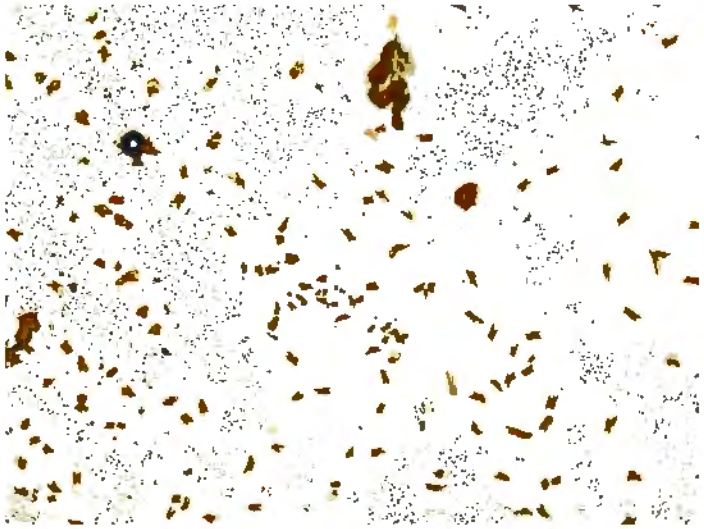


Figure 7. 1 PPP from a 50 mg tramadol tablet in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form rectangular plates, bowties and X shapes. Crystals form parallelograms and rectangular plates.

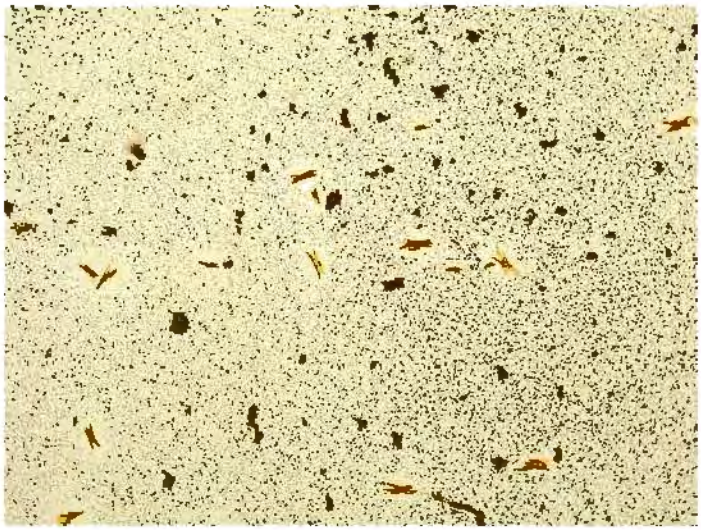


Figure 8. 2 PPP from a 37.5 mg tramadol and 325 mg acetaminophen in 2 µL of H_2O and 10 µL of $HAuBr_4$ with HOAc and (2+3) H_2SO_4 reagent, with coverslip. Crystals form bow ties and X-shaped crystals..

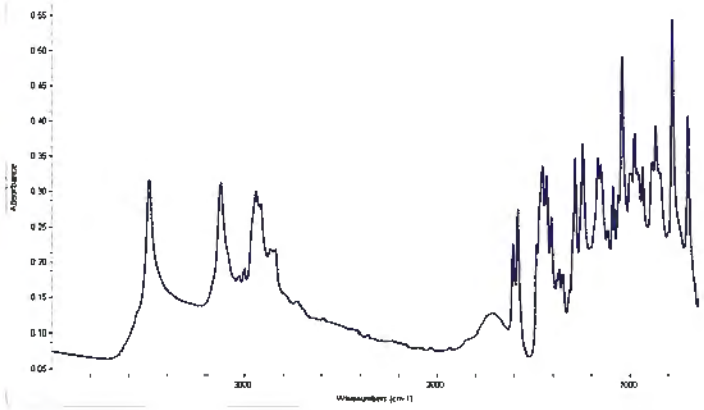


Figure 9. Infrared spectrum of tramadol gold bromide with acetic acid and sulfuric acid precipitate. Download/view SPC file

Tramadol: Gold Bromide with Hydrochloric Acid

REAGENT 1B: Gold Bromide ($HAuBr_4$) with Concentrated Hydrochloric Acid (HCl)

There are two ways to make this reagent: 1.3 g $HAuBr_4$ in concentrated HCl, make up to 30 mL. Alternatively, to convert gold chloride to gold bromide: 1 g $HAuCl_4 \cdot 3H_2O$ and 1.5 mL HBr (40%) in concentrated HCl, make up to 30 mL. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Add 10 µL of the reagent to a coverslip. Invert the coverslip and place it directly onto the sample on a glass slide.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈5–10 minutes

Crystal Morphology and Test Notes

Rosettes of blades, which become larger over time.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of tramadol in 10 µL of $HAuBr_4$ with HCl reagent. Crystals form rosettes of blades.

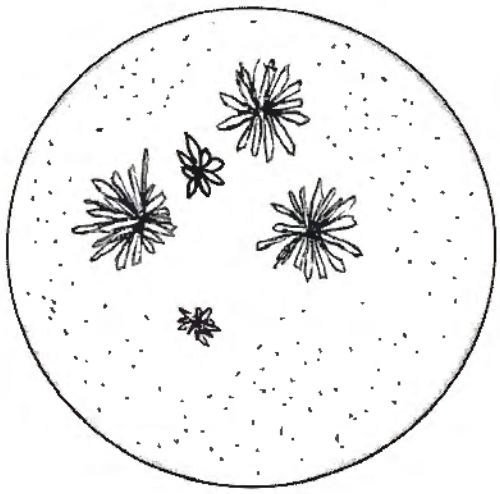
Pharmaceuticals, Adulterants, or Other Drug Interactions

This test was successful on pharmaceutical tablets from two manufacturers (Apotex® and Kali®), each containing 37.5 mg of tramadol and 325 mg of acetaminophen using 4 PPPs. It was also successful on tablets from two other manufacturers (McNeil®and Mylan®), each containing 50 mg of tramadol using 2 PPPs, and on a tablet (Patriot®) containing 100 mg of tramadol using 1 PPP; no extraction procedures were necessary. Note: Acetaminophen forms colorless, angular plates and clusters of plates in 10 µL of $HAuBr_4$ with HCl reagent, distinguishable from tramadol (see Figure 9).

IR Spectrum

See Figure 10. Download/view SPC file

PLM Optical Properties

Approximate Size Range	10–60 µm
Color/Pleochroism	Yellow-orange. Pleochroic: light yellow to orange
Refractive Indices (RI)	> 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Room temperature
Estimated Birefringence	Low
Extinction	Parallel (needles)
Sign of Elongation	Needles: positive (+); Blades: positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Likely biaxial

Tramadol: Gold Bromide with Hydrochloric Acid (continued)

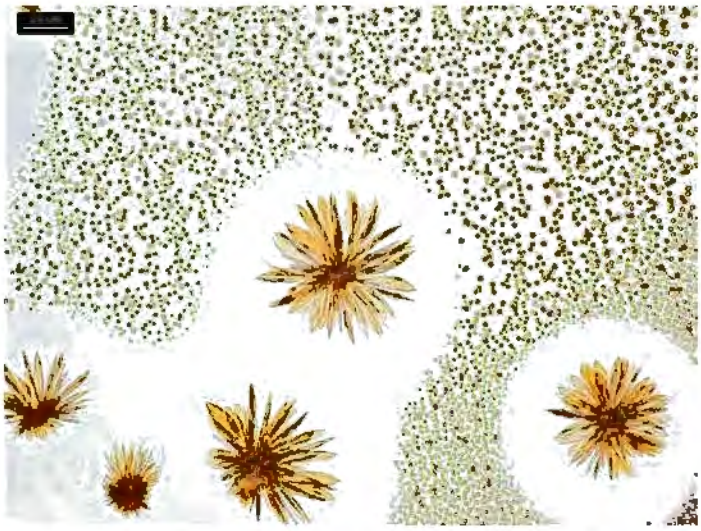


Figure 2. 1 PPP of tramadol in 10 µL of $HAuBr_4$ with HCl reagent. Crystals form rosettes of blades.

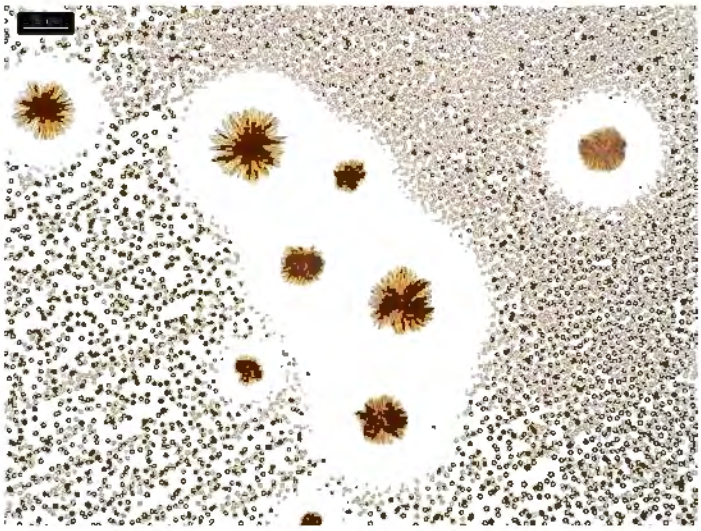


Figure 3. 1 PPP of tramadol in 10 µL of $HAuBr_4$ with HCl reagent. Crystals form rosettes of blades.

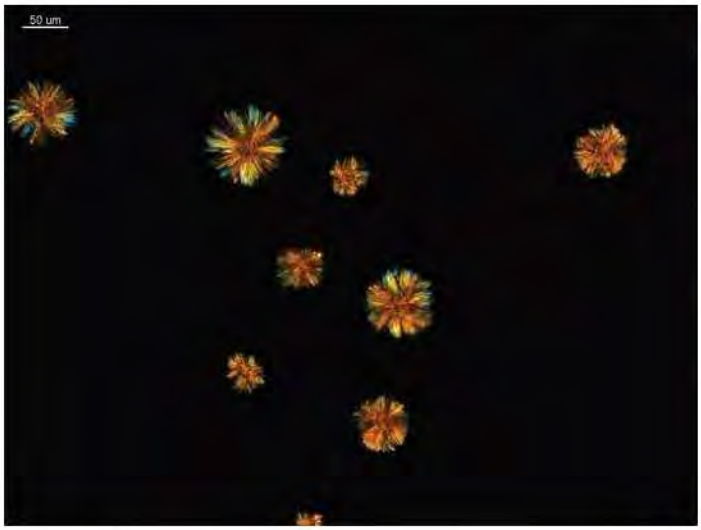


Figure 4. Same as Figure 3; crossed polars.

Figure 5. Same as Figure 3; crossed polars and Red I compensator.

Tramadol: Gold Bromide with Hydrochloric Acid (continued)

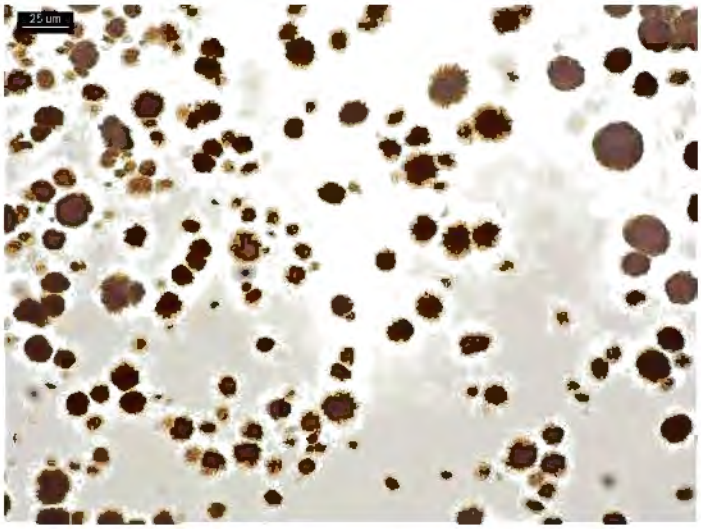


Figure 6. 1 PPP from a 100 mg tramadol tablet in 10 µL of $HAuBr_4$ with HCl reagent, with coverslip. Crystals form rosettes of blades.

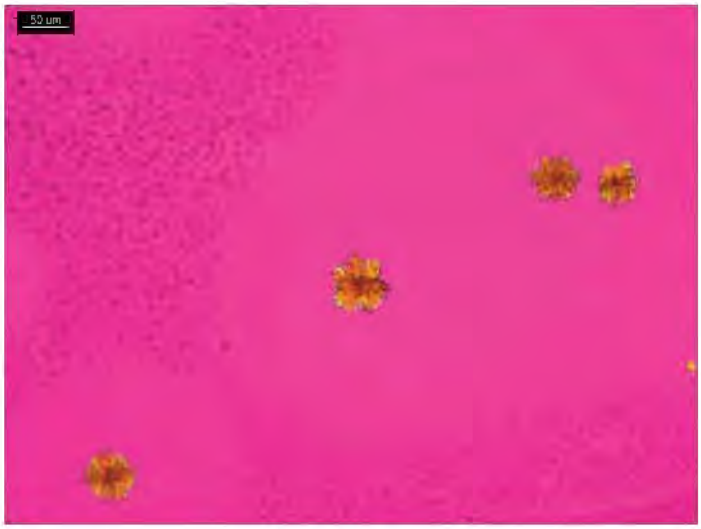


Figure 7. 2 PPP from a 50 mg tramadol tablet in 10 µL of $HAuBr_4$ with HCl reagent, with coverslip. Crystals form rosettes of blades.

Figure 8. 4 PPP from a 37.5 mg tramadol and 325 mg acetaminophen tablet in 10 µL of $HAuBr_4$ with HCl reagent, with coverslip. Crystals form rosettes of blades.

Figure 9. Acetaminophen forms colorless, angular plates and clusters of plates in 10 µL of $HAuBr_4$ with HCl reagent, distinguishable from tramadol.

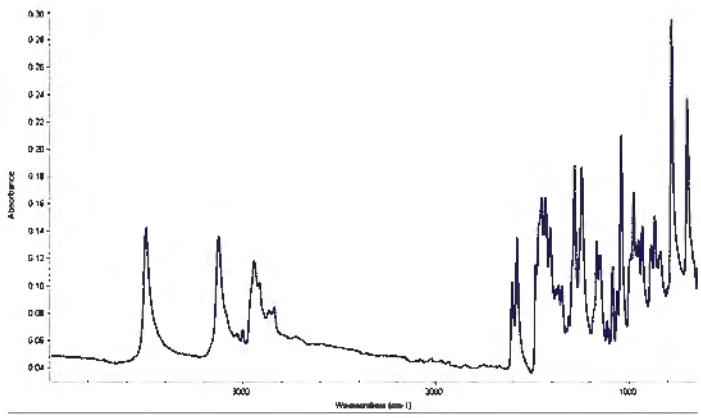


Figure 10. Infrared spectrum of tramadol gold bromide with hydrochloric acid precipitate. Download/view SPC file

Zolpidem: Gold Chloride with Hydrochloric Acid

REAGENT 1: Gold Chloride ($HAuCl_4$) with Hydrochloric Acid ((1+3) HCl)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+3) HCl, make up to 20 mL. (1+3) HCl is dilute hydrochloric acid made by combining one part (e.g. 5 mL) of concentrated hydrochloric acid with three parts (e.g. 15 mL) water.

Test Method

Direct test: Dissolve sample in 2 µL of 10% HCl. Add 5 µL of the reagent to a coverslip. Invert the coverslip and place it directly onto the sample on a glass slide. Alternatively, dissolve sample in 2 mL of 10% HCl, add 5 µL of the reagent directly to the sample on a glass slide; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈4 minutes

Crystal Morphology and Test Notes

Burrs, clusters, rosettes, and sheaves.

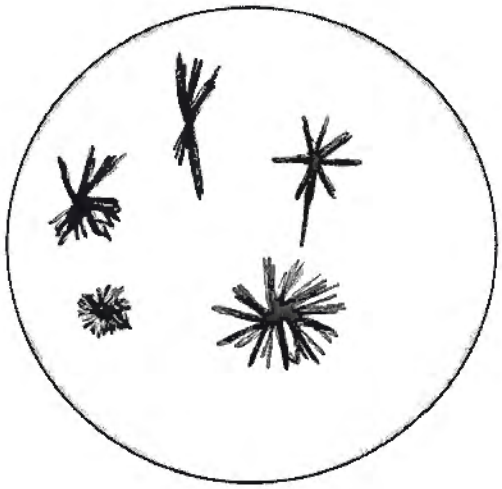
Photomicrograph of Typical Crystals

Figure 1. 1 PPP of zolpidem in 2 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent. Crystals form burrs, clusters, rosettes, and sheaves.

Pharmaceuticals, Adulterants, or Other Drug Interactions

This test was successful on a 5 mg zolpidem tartrate pharmaceutical tablet (NorthStar®) using 3 PPP and on a 5 mg/0.1 mL oral spray solution (Zolpimist®) using 2 µL. Tests were also successful on a 1.75 mg sublingual pharmaceutical tablet (Intermezzo®) and a 6.25 mg extended release tablet (Sandoz®), but required an extraction procedure: using ¼ of a tablet, add the crushed inner portion to a microcentrifuge tube, add 200 µL of absolute ethanol, then stir well with a pipette tip, and allow to sit for 30 minutes. Shake gently, then centrifuge for 1 minute or until there is a clear separation of liquid and solid. Extract 40 µL with a micropipette and drop onto a glass slide in four 10 µL increments, allowing each drop to dry before adding the next drop. Dissolve sample in 2 µL of 10 % HCl. Add 5 µL of the reagent to a coverslip. Invert the coverslip and place it directly onto the sample on a glass slide. Using a pencil eraser, apply pressure to the coverslip and slide it forward once in order to form crystals.

PLM Optical Properties

Approximate Size Range	10–70 µm
Color/Pleochroism	Light brown; not pleochroic
Refractive Indices (RI)	n-parallel ≈1.660 n-perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Room temperature
Estimated Birefringence	Moderate–High
Extinction	Oblique
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Zolpidem: Gold Chloride with Hydrochloric Acid (continued)

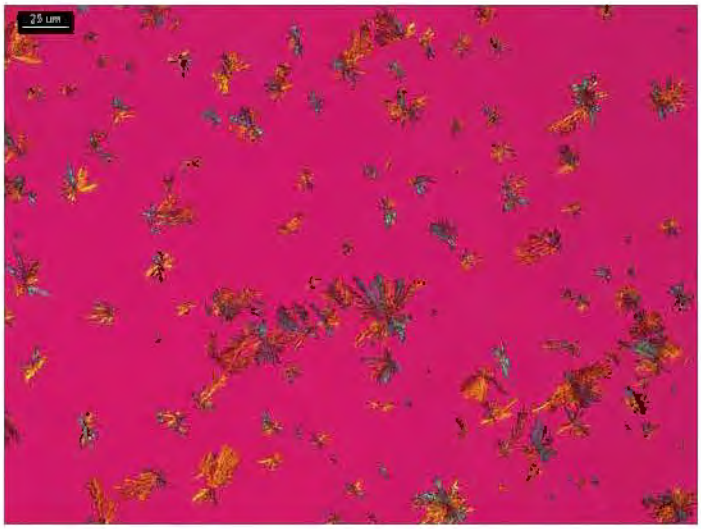


Figure 2. 1 PPP of zolpidem in 2 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent. Crystals form burrs, clusters, rosettes, and sheaves; crossed polars and Red I compensator.

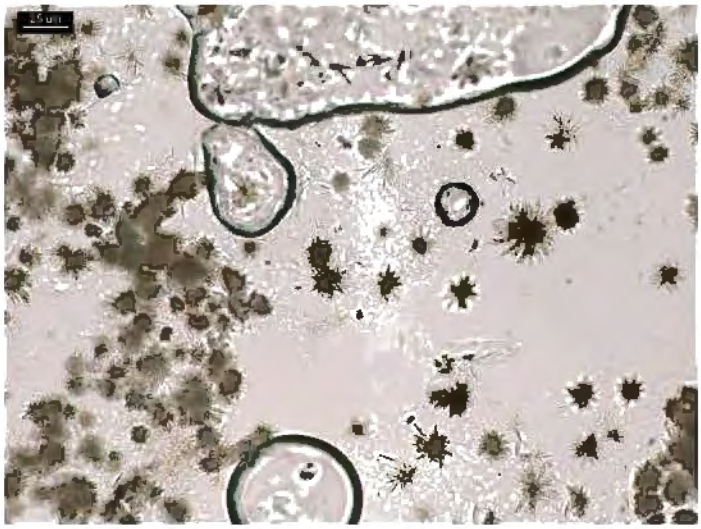


Figure 3. 40 µL from a 6.25 mg extended release pharmaceutical tablet after extraction procedure in 2 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent. Crystals form burrs, clusters, and rosettes.

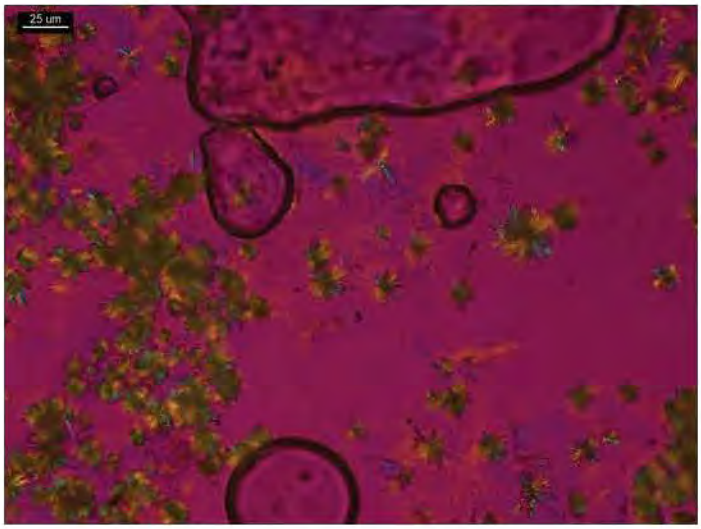


Figure 4. Same as Figure 3; crossed polars and Red I compensator.

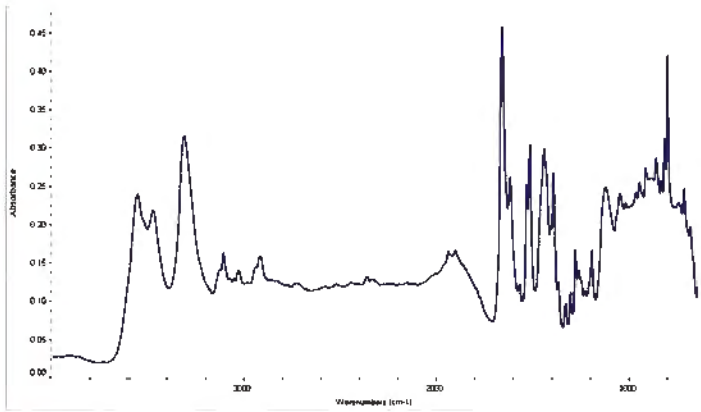


Figure 5. Infrared spectrum of zolpidem gold chloride with hydrochloric acid precipitate.

Zolpidem: Platinum Bromide with Sulfuric Acid

REAGENT 2: Platinum Bromide (H_2PtBr_6) with Sulfuric Acid ((2+3) H_2SO_4)

There are two ways to make this reagent: 1.3 g H_2PtBr_6 in (2+3) H_2SO_4, make up to 20 mL. (2+3) H_2SO_4 is dilute sulfuric acid made by combining two parts (e.g. 8 mL) of concentrated sulfuric acid with three parts (e.g. 12 mL) of water. Alternatively, to convert platinum chloride to platinum bromide: 1 g $H_2PtCl_6 \cdot 6H_2O$ and 1.7 mL HBr (40%) in (2+3) H_2SO_4, make up to 20 mL. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Dissolve sample in 2 µL of 10% H_2SO_4. Add 5 µL of the reagent to a coverslip. Invert the coverslip and place it directly onto the sample on a glass slide. Alternatively, add 5 µL of the reagent directly to the sample on a glass slide; no coverslip.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Sheaves, cornstalk- and jagged X-shaped crystals. Some of the larger sheaves form fans.

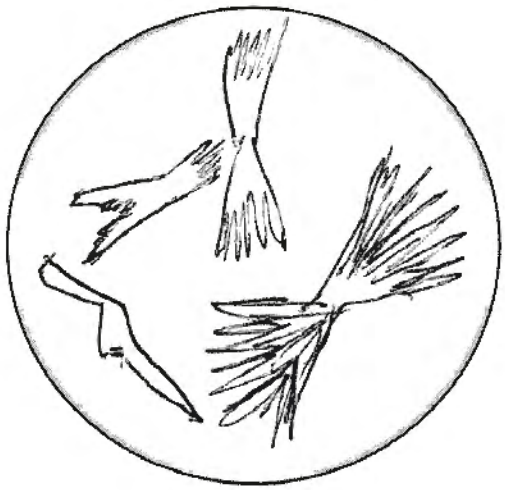
Photomicrograph of Typical Crystals

Figure 1. 1 PPP of zolpidem in 2 µL of 10% H_2SO_4 with 2 µL of H_2PtBr_6 reagent. Crystals form sheaves and cornstalk-shaped crystals.

Pharmaceuticals, Adulterants, or Other Drug Interactions

This test was successful on a 5 mg zolpidem tartrate pharmaceutical tablet (NorthStar®) using 3 PPP and on a 5 mg/0.1 mL oral spray solution (Zolpimist®) using 2 µL. Tests were also successful on a 1.75 mg sublingual pharmaceutical tablet (Intermezzo®) and a 6.25 mg extended release tablet (Sandoz®), but required an extraction procedure: using ½ of a tablet, add the crushed inner portion to a microcentrifuge tube, add 200 µL of absolute ethanol, then stir with a pipette tip, and allow to sit for 90 minutes. Shake gently, then centrifuge for 1 minute or until there is a clear separation of liquid and solid. Extract 40 µL with a micropipette and drop onto a glass slide in four 10 µL increments, allowing each drop to dry before adding the next drop. Dissolve sample in 2 µL of 10% H_2SO_4. Add 5 µL of the reagent to a coverslip. Invert the coverslip and place it directly onto the sample on a glass slide. Using a pencil eraser, apply pressure to the coverslip and slide it forward once in order to form crystals.

PLM Optical Properties

Approximate Size Range	20–500 µm
Color/Pleochroism	Yellow; not pleochroic
Refractive Indices (RI)	n >1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Washed with water, then excess liquid was wicked away with lab tissue and dried at room temperature.
Estimated Birefringence	Moderate–High
Extinction	Oblique
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Zolpidem: Platinum Bromide with Sulfuric Acid (continued)

Figure 2. 1 PPP of zolpidem in 2 µL of 10% H_2SO_4 with 2 µL of H_2PtBr_6 reagent. Crystals form sheaves and jagged X shapes.

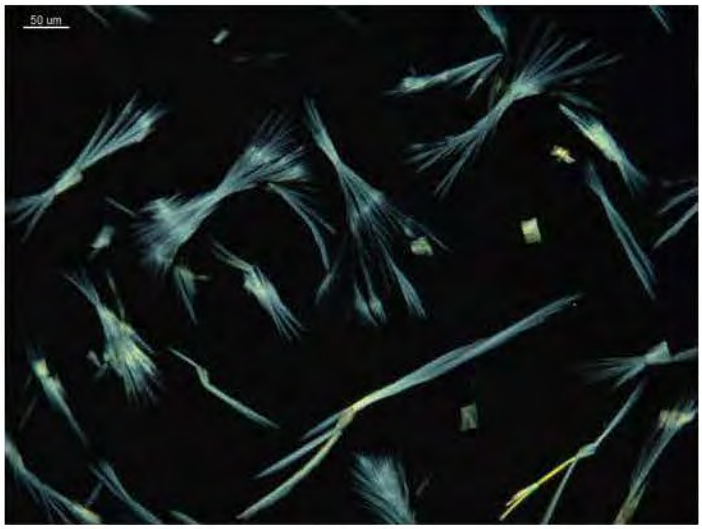


Figure 3. 1 PPP of zolpidem in 2 µL of 10% H_2SO_4 and 5 µL of H_2PtBr_6 reagent. Crystals form sheaves and cornstalk-shaped crystals; crossed polars.

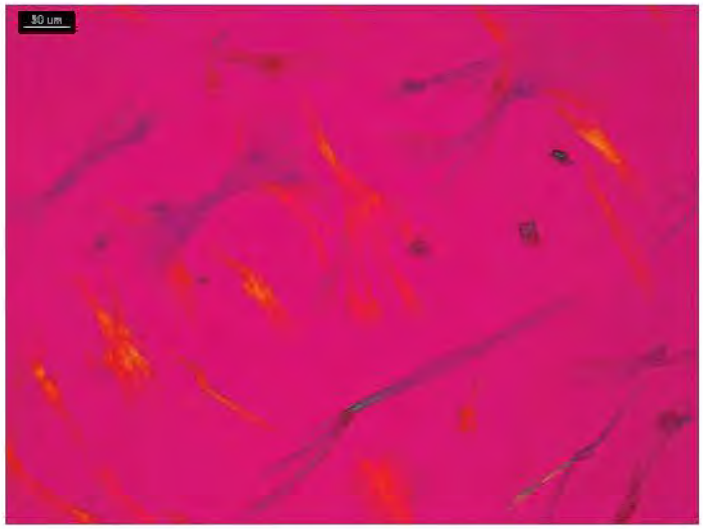


Figure 4. Same as Figure 3; crossed polars and Red I compensator.

Figure 5. 2 µL of zolpidem from an oral spray solution (5 mg/0.1 mL) in 2 µL of 10% H_2SO_4 and 5 µL of H_2PtBr_6 reagent. Crystals form sheaves and jagged X shapes.

Zolpidem: Platinum Bromide with Sulfuric Acid (continued)

Figure 6. 40 µL from a 1.75 mg sublingual zolpidem pharmaceutical tablet after extraction procedure in 2 µL of 10% H_2SO_4 and 5 µL of H_2PtBr_6 reagent. Crystals form sheaves and jagged X shapes.

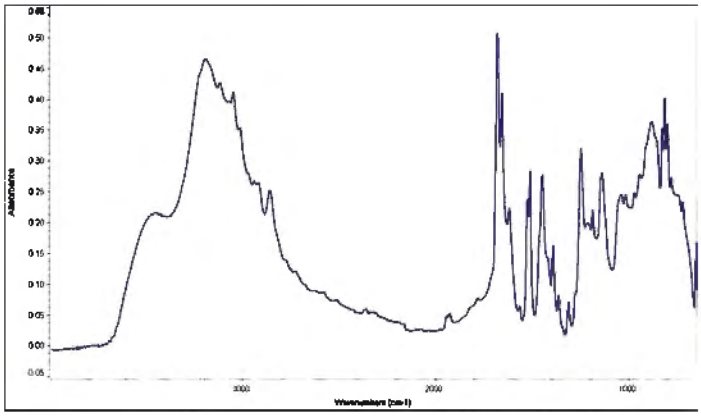


Figure 7. Infrared spectrum of zolpidem platinum bromide with sulfuric acid precipitate.

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