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A Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals

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A Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals

Kelly M. Brinsko, M.S.[1], Dean Golemis, B.A.[1], Meggan B. King, B.S.[1], Gary J. Laughlin, Ph.D.[1] and Sebastian B. Sparenga, M.S.[1]

Summary

This document presents "A Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals" for use by forensic scientists in the crime laboratory and researchers in the analytical chemistry laboratory.

Background

An ideal microanalytical method for forensic drug analysis would be inexpensive, fast, automated and suitable for all known drugs; however, no such tool currently exists. Traditional light microscopy and microcrystal tests have been used together for more than 100 years, and are proven useful when automated instrumental analysis is unavailable or not appropriate, if mixtures of one or more drugs, excipients, diluents or adulterants are present, or when the drug is held in alternative delivery devices such as gels or transdermal patches. Furthermore, while some crime laboratories may lack certain automated instrumental capabilities, most have light microscopes and properly trained microscopists. Microcrystal tests, using polarized light microscopy (PLM), can identify most illicit drugs specifically and quickly (usually within a few minutes), and they are inexpensive compared to other methods. In addition, proper use of the light microscope and microcrystal tests can check and confirm the results obtained by alternative methods. It is envisaged that this compendium will fulfill a critical need for reliable analytical methods and assist forensic scientists and other researchers in their work.

Microcrystal Tests

"A Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals" contains 19 drugs for which microcrystal tests using various reagents have been previously developed. It describes in detail the microcrystals formed from each test and includes photomicrographs, morphology illustrations, optical properties, notes and infrared (IR) spectra of the microcrystals.

The 19 drugs chosen for inclusion in the compendium were selected from annual reports compiled by the National Forensic Laboratory Information System (NFLIS). The reports issued by NFLIS describe in detail the controlled substances that are identified by federal, state and local forensic laboratories across the United States. The NFLIS reports also include the national estimates for the 25 most frequently reported drugs, along with observed trends. Of these 25 drugs, 18 already have known, published microcrystal tests. The 19th drug, ephedrine, was added to this compendium because of its prevalence as a precursor in clandestine methamphetamine laboratories.

Information about known microcrystal tests and reference material from numerous sources spanning past decades, including textbooks, journal articles and standard operating procedures, were located and evaluated. Many of these are out of print and not easily accessible. Such references typically contain few photomicrographs of microcrystals, and their reagent formulations and procedures may be difficult to interpret. There is also a lack of information regarding potential interferences from other drugs that may be combined with pharmaceuticals or from adulterants found in street drug samples.

A survey of crime laboratories was conducted to determine which reagents and microcrystal tests are currently in use. Because the literature contains numerous microcrystal tests that could be used to identify a single compound, it is most efficient to compile only the most commonly used protocols within the compendium. This

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approach has several advantages: Presumably, the popularity of a test is indicative of its expediency. After decades of use, less expedient microcrystal tests have been eradicated or modified in favor of more reliable and/or more sensitive ones. Compiling and ranking this data is an efficient way to evaluate the use and reputation of certain microcrystal tests. By including the most commonly used microcrystal tests utilized by many forensic laboratories makes it less complicated for individual laboratories to amend their current procedures. It also ensures that the reagents used in the tests are accessible and available.

Most drugs in this compendium include two or three reagents that may be used for their identification; in a few cases, only one reagent is provided. These drugs may have had only one previously published reagent, or may have had additional reagents that were found to be unreliable, inaccessible or impractical.

Techniques have also been developed for drugs with non-traditional delivery mechanisms, including gels and transdermal patches. All procedures were vetted and evaluated by McCrone Research Institute research microscopists, together with practicing forensic scientists in other collaborative laboratories. The compendium includes recommended protocols, reagents, morphology of crystals (with numerous photomicrographs), IR spectra of microcrystals, and potential interferences. In addition, the compendium includes optical and crystallographic properties of the microcrystals. Optical properties are not included in many references, which is unfortunate because microcrystals are unique when they are presented together with morphology. By including the optical data in the compendium, the application of many microcrystal tests is refined, which potentially strengthens their use within the criminal justice system.

The compendium includes the following topics for each drug: reagents; test methods; sensitivity of the test and limit of detection; time required for crystal formation; crystal morphology; evaluation of the tests in the presence of common excipients, diluents and adulterants (for street drug samples) or combination drugs (for pharmaceutical preparations); and evaluation of the tests for drugs from selected pharmaceutical delivery devices, e.g. tablets, capsules, gels, transdermal patches and oral solutions.

Limit of Detection

The limit of detection (LOD) or minimum amount of sample required to obtain a positive result, i.e., typical crystal formation, was determined for each drug and reagent in the compendium. Some previous researchers referred to using samples “the size of a period on a printed page.” The amount suggests a minimum required sample quantity and provides a means to compare the sensitivity of all the microcrystal tests. An analogous unit of measurement was established for this compendium wherein sample size was measured in units of "PPP," a quantity with an approximate diameter the size of a single period on a printed page. This unit represents a quantity of sample that fills the area of a period printed or displayed at 100% and Times New Roman 10-point font. The weight of 1 PPP is approximately 0.1 mg. All microcrystal tests in the compendium specify a LOD (usually 1 PPP) for each drug and reagent; however, the LOD is a lower limit and more material can be tested with similar results. Pharmaceutical products included in the compendium were tested at various dosages or concentrations and in most cases, the lowest dosage pharmaceutical and the lowest quantity of material required for a successful test was specified.

Crystal Morphology

Descriptions of typical crystal morphology were often used in reference to Clarke (Figure 1). There are some cases where Clarke’s general descriptions are used with additional terms for microcrystals that resemble easily recognizable objects: parallelograms, nails, bow ties, coffins, dahlia flowers, pants, wrapped candy, etc.

Pharmaceuticals, Adulterants, Other Drug Interactions and Alternative Delivery Devices

The compendium includes commonly encountered adulterants and excipients that were tested in several ratios with the drugs (5:1, 1:1 and 1:5) to determine the success of each microcrystal test and reagent. In most cases, the microcrystal test was successful and the drug was detected in these ratios. However, in a few cases, the drug produced no crystals, was not reproducible, or did not produce typical crystals in the presence of the adulterant or excipient. Some pharmaceuticals included several different drugs or ingredients, and the additional drugs interfered with the microcrystal test, or the drug was present in such low concentration that typical crystals were distorted or did not form. In these instances, micro-scale extractions were performed in order to extract, isolate or concentrate the drug. The extractions carried out using microcentrifuge tubes take only a few minutes and are described in the compendium.

In addition to tablets and capsules, several pharmaceuticals employing alternative delivery devices (e.g. oral solutions, extended-release formulations, gels and transdermal patches) were tested in order to determine the suc-

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cess or failure of the microcrystal tests. In some cases, the microcrystal test produced no positive results directly, and micro-scale extractions were required. After some modifications to the test methods, many microcrystal tests were successful on alternative delivery devices and described in the compendium.

Fourier Transform Infrared Microspectroscopy

Infrared spectra of the microcrystals obtained by Fourier-transform IR microspectroscopy were not available in any of the references and are now included in this compendium. It was observed that the spectra obtained from the drugs are different than the spectra obtained from typical microcrystals of the same drug. There are sometimes differences in peaks and small shifts in peak positions, and there are differences that may occur in the spectra of microcrystals for the same drug when using different reagents.

IR spectra files (.spc) for microcrystal tests are available for download by clicking the caption or spectrum figure in the compendium, or on the McCrone Research Institute website, www.mcri.org.

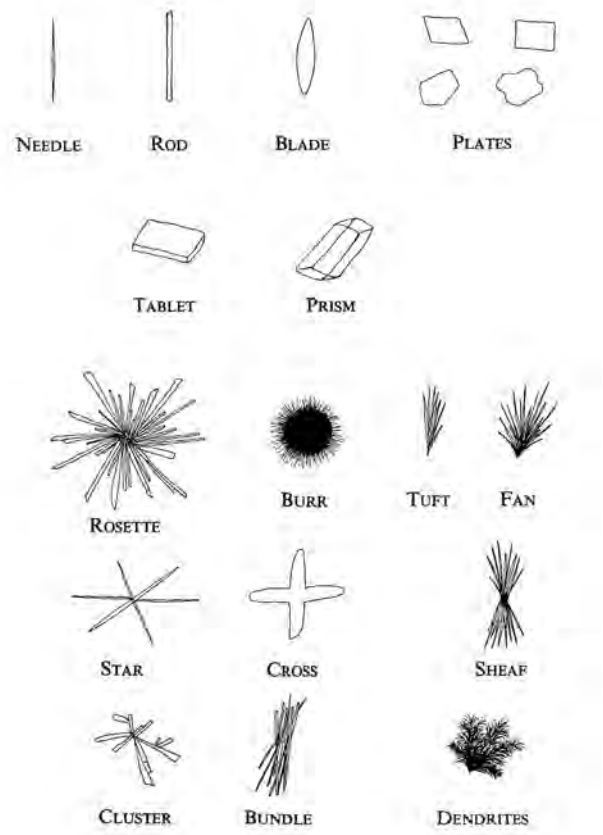

Figure 1. Microcrystal morphology (from Clarke; used with permission).

PLM Optical Properties

Refractive Indices

The refractive indices of some microcrystals were difficult to determine because they must be dried, not obscured by recrystallized reagent, and excess liquid must be wicked away before applying the refractive index liquids. Crystals in ordinary aqueous reagents were most easily dried at room temperature, while those in acidic reagents needed to be washed with a solvent, such as ethanol or chloroform, then dried. The following is the procedure used for washing the crystals: Excess reagent was wicked with a lab tissue or filter paper. A drop of solvent was placed on a slide near the typical crystals that formed, then a tungsten needle was used to wick up some of the solvent to draw it over the crystals and wash free the reagent from the crystals. This may require multiple attempts to sufficiently remove the reagent. Some of the microcrystals have refractive indices greater than 1.700, which are considered very high refractive indices and are above the limit at which many laboratories are capable of determining with readily available refractive index liquids. When microcrystals exhibited a refractive index greater than 1.700, this result was recorded, and exact values were not pursued further.

Estimated Birefringence

Birefringence (B) was determined by measuring the thickness of the crystal using a calibrated ocular scale and estimating the interference colors observed in crossed polars with PLM. The birefringence was then calculated using a Michel-Lévy interference color chart or the classic birefringence equation, $B = R / (1000 \times T)$, where R is retardation (interference color value, in nanometers) and T is crystal thickness (in micrometers). Birefringence for the typical microcrystals was estimated to be low when the values were less than 0.010, moderate when they were between 0.010 and 0.050, or high when they were greater than 0.050.

Sign of Elongation

The sign of elongation was determined for microcrystals that are elongated. If the refractive index parallel to the long axis (length) is greater than the refractive index perpendicular to the long axis (width), then the crystal has a positive sign of elongation. If the opposite is true, it has a negative sign of elongation.

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Interference Figures

Interference figures were difficult to obtain on the microcrystals. Many of the microcrystals were not a suitable shape or size or were not properly oriented to observe an interference figure. However, there are a few crystals in the compendium that did show good interference figures. When an interference figure was observed, its uniaxial or biaxial character was recorded together with the optic sign.

Methods and Technical Notes

The procedures used throughout the compendium are standard procedures employed by most microscopy laboratories and will be familiar to any microscopist. Techniques that may be less common (e.g. the "hanging drop" method used after volatilizing certain drugs) are explained in the appropriate section for each drug. However, there are technical details about the tests throughout the compendium that should be noted: Most microcrystal tests are performed in an exposed reagent drop without using a coverslip. Unless specified, a coverslip was not used in performing these tests. Occasionally, a coverslip was placed on the reaction drop after crystal growth occurred, in order to obtain better quality photomicrographs.

Most of the microcrystal tests in this compendium required less drug material and, therefore, less liquid reagent than traditional laboratory dropper bottles provide. A micropipette was used to obtain smaller quantities of liquid. However, if a micropipette is not available, tiny drops of solvent or reagent can be made by using a tapered glass rod. A tapered glass rod is made from a length of cylindrical glass approximately 10 cm in length and 2–3 mm in diameter that has been drawn out in a flame to about 1 mm diameter at the tip, then polished to a flat, blunt end. The glass rod can be used to obtain small drops of solvent or reagent by simply teasing a drop from a bottle dropper. The bottle dropper is squeezed slightly, allowing a small amount of liquid to exit the tip as the glass rod is drawn across the opening. This creates a micro-drop, approximately 5 µL, on the tip of the glass rod. The drop can then be placed on a glass slide or coverslip in preparation for the microcrystal test. A 5 µL drop, after being placed on the glass slide or coverslip, will be about 5 mm in diameter.

Glass rings, used during the volatility tests have the following specifications: 17 mm outer diameter; 14 mm inner diameter; 1 mm wall thickness; 5 mm height. Different diameter rings and glass concavity slides should give similar results, however, the microscope may have difficulty focusing with glass rings more than 5 mm in height, especially when using high magnification objectives. Glass is the preferred material for the rings because it is inert, however, other materials may be substituted if they will not interfere with the microcrystal tests.

Reagent formulations are written using the quantities given in the original sources but can be halved, quartered or otherwise adjusted as needed. Unless otherwise noted, the reagents are stable for years if stored properly. However, if the age or condition of a reagent is uncertain, the test should be performed on a known drug sample to ensure the reagent is working properly.

Data in the compendium, including the photomicrographs, were obtained using research-grade drug standards in order to acquire the highest quality results. Pharmaceuticals and street drug samples tested with the reagents typically yielded the same microcrystals. However, in some rare cases, certain combination drugs or adulterants may have caused the test to be unsuccessful. These instances are noted in the appropriate drug and reagent sections, together with any alternative test methods.

Pharmaceutical tablets are often coated or encapsulated with inert ingredients that do not contain any drug material. Therefore, when sampling from a pharmaceutical tablet, the tablet was first broken in order to expose the inner portion. A needle or sharp instrument was then used to break off small pieces from the center, leaving the coating behind. The drug material is sometimes present as colorless particles, which can be distinguished from other fillers and binders (e.g. microcrystalline cellulose, starch, etc.), when using a stereomicroscope. The drug particles may be euhedral (well-formed), causing them to appear shiny in reflected light. When these crystals are present, they should be selected and removed individually for the microcrystal tests.

Conclusion

"A Modern Compendium of Microcrystal Tests for Illicit Drugs and Diverted Pharmaceuticals" is presented in a PDF file and comprises 19 drugs. It includes reagents, microcrystal test methods, optical properties and IR spectra. This compendium will remain a work-in-progress and be updated with additional drugs, reagents and microcrystal tests once such data become available.

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Author Contributions

Kelly Brinsko, Meggan King and Sebastian Sparenga performed and evaluated the microcrystal tests, documented the optical properties, and assisted in the format, layout and design of the compendium. Sparenga performed the IR microspectroscopy. Dean Golemis designed the layout, created the pages and edited the content. Gary Laughlin provided the editorial and technical review and overall project management. All authors read and approved the final document.

Acknowledgments

The authors would like to thank James Dunlop (Kalamazoo County Sheriff's Office), Hiram Evans (San Bernardino County Sheriff's Department, Retired) and Skip Palenik (Microtrace, LLC) for their advice and assistance throughout this project.

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d-Amphetamine: Gold Chloride

REAGENT 1: Gold Chloride ($HAuCl_4$)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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

There are two test methods, volatility and direct; both give the same crystals. Volatility tests are preferred for pharmaceutical tablets.

Volatility test: With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring. If after 5 –20 minutes, oily drops form at the edge of hanging drop, then remove coverslip and place faceup to expose drop to air; once faceup, crystals should form within 5 minutes. However, if after 5–20 minutes, oily drops do not form in hanging drop, the test is unlikely to produce any crystals, even when the coverslip is faceup.

Direct test: Dissolve sample in 5 µL of concentrated phosphoric acid, then add 5–10 µL of reagent; gentle stirring is optional.

References

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2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.

Limit of Detection

2 PPP for both test methods

Time Required for Crystal Formation

Volatility: 5 minutes
Direct: Immediate

Crystal Morphology and Test Notes

Long yellow rods form, which are sometimes stacked, segmented and serrated. The ends are blunt, slightly angled or tapered.

Photomicrograph of Typical Crystals

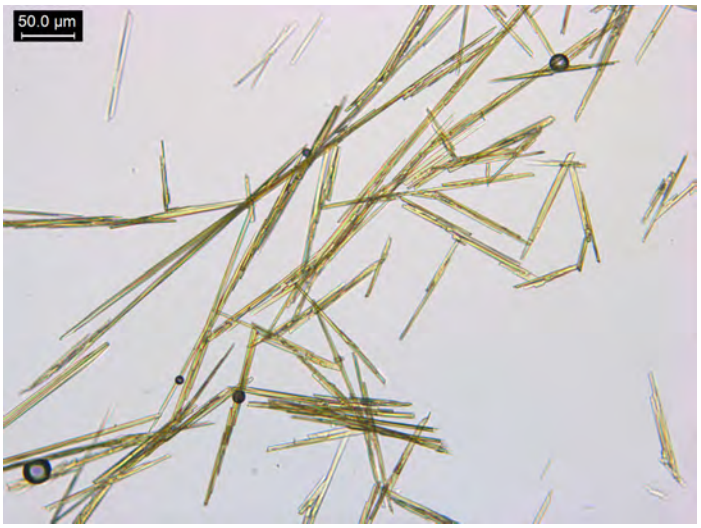
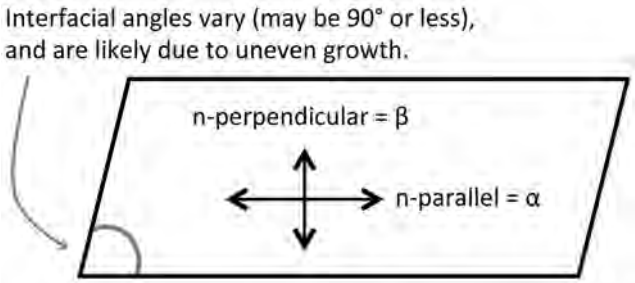


Figure 1. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

Pharmaceuticals, Adulterants or Other Drug Interactions

This microcrystal test was successful on one crushed prill (≈2 PPP) from a 10 mg capsule and on one crushed prill (≈2 PPP) from a 10 mg "XR" extended release formulation.

PLM Optical Properties

Approximate Size Range	10 µm to > 1 mm length
Color/Pleochroism	Yellow; not pleochroic
Refractive Indices (RI)	n-parallel = 1.658 n-perpendicular > 1.700
Morphology Illustration	
How Crystals Were Dried for RI Measurement	Excess liquid was wicked with lab tissue then washed with chloroform using a tungsten needle.
Estimated Birefringence	Moderate
Extinction	Parallel only
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Biaxial, positive (+), 2V ≈ 64°

IR Spectrum

See Figure 16. Download SPC file.

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d-Amphetamine: Gold Chloride (continued)

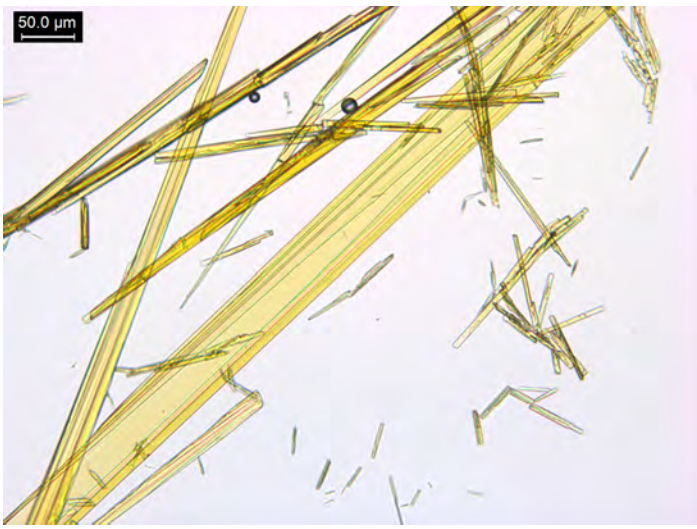

Figure 2. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

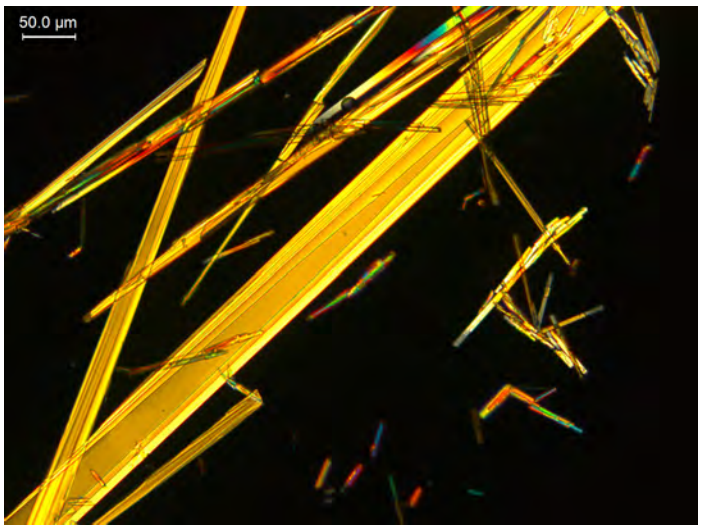

Figure 3. Same as Figure 2; crossed polars.

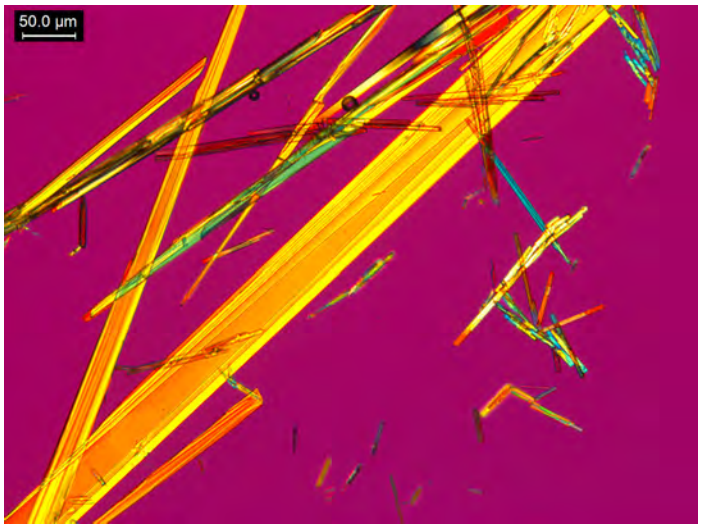

Figure 4. Same as Figure 2; crossed polars and Red I compensator.

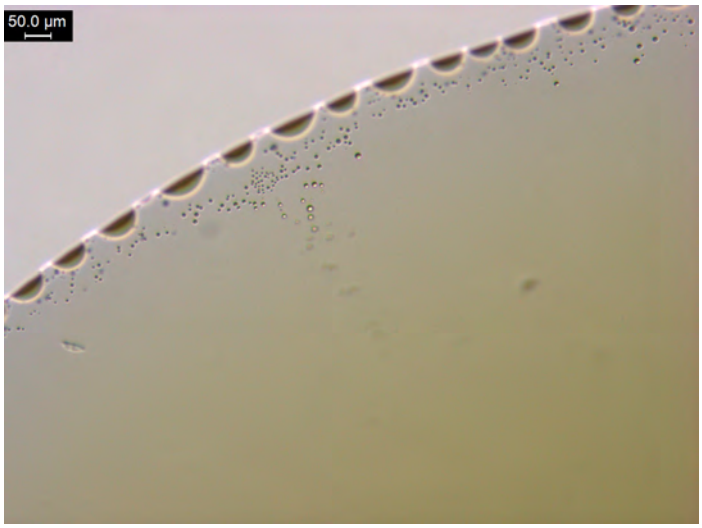

Figure 5. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; in a 5 µL hanging drop of $HAuCl_4$ reagent. Immiscible oily drops form at the edge of the hanging drop within 5 minutes after adding NaOH to the sample. These oily drops immediately precede crystal formation.

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d-Amphetamine: Gold Chloride (continued)

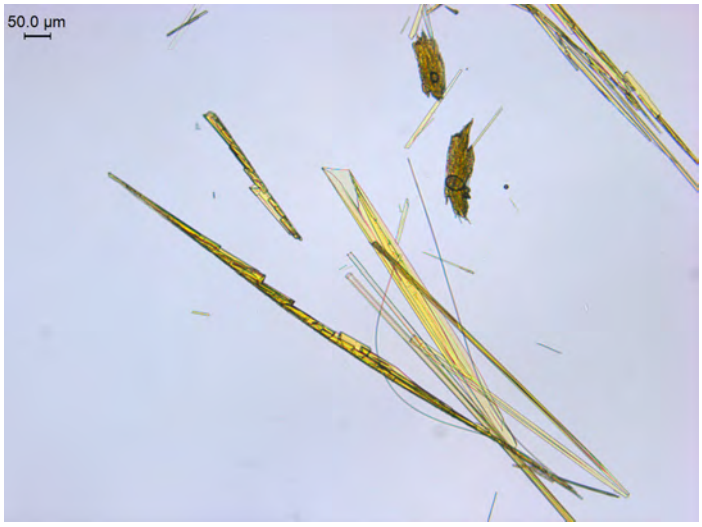

Figure 6. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods. Note the segmented and serrated morphology in some crystals.

Figure 7. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

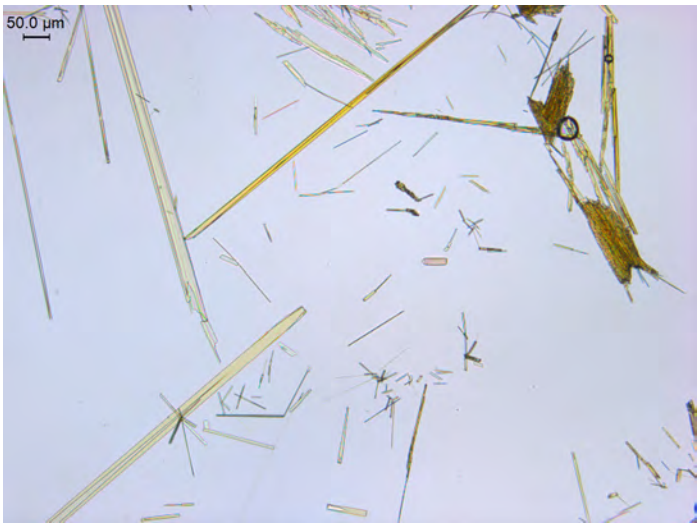

Figure 8. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

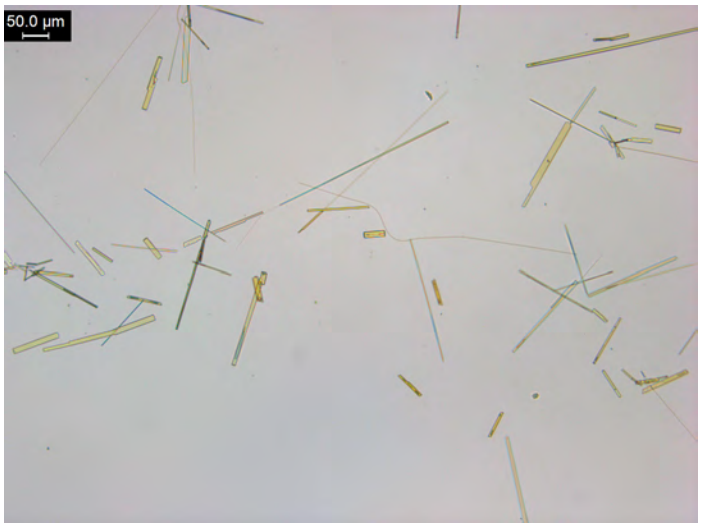

Figure 9. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

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d-Amphetamine: Gold Chloride (continued)

Figure 10. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form stacked and segmented long yellow rods.

Figure 11. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent. Crystals form long yellow rods.

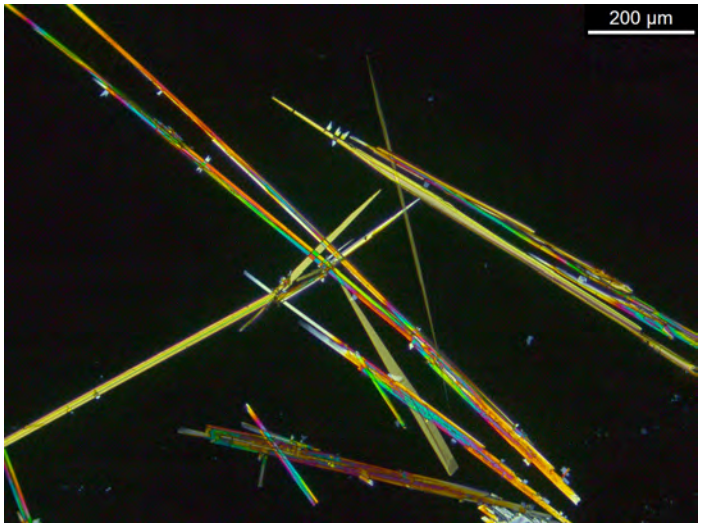

Figure 12. Same as Figure 11; crossed polars

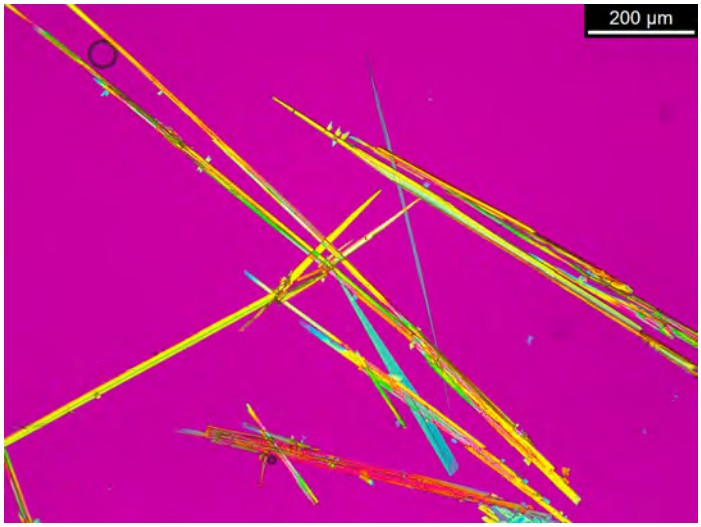

Figure 13. Same as Figure 11; crossed polars and Red I compensator.

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d-Amphetamine: Gold Chloride (continued)

Figure 14. Direct test: 2 PPP of *d*-amphetamine dissolved in 2 µL of concentrated H_3PO_4, and 10 µL of $HAuCl_4$ reagent; crystals form instantly. Crystals form long yellow rods. After the crystals formed, a coverslip was placed on the sample to flatten it for this photomicrograph.

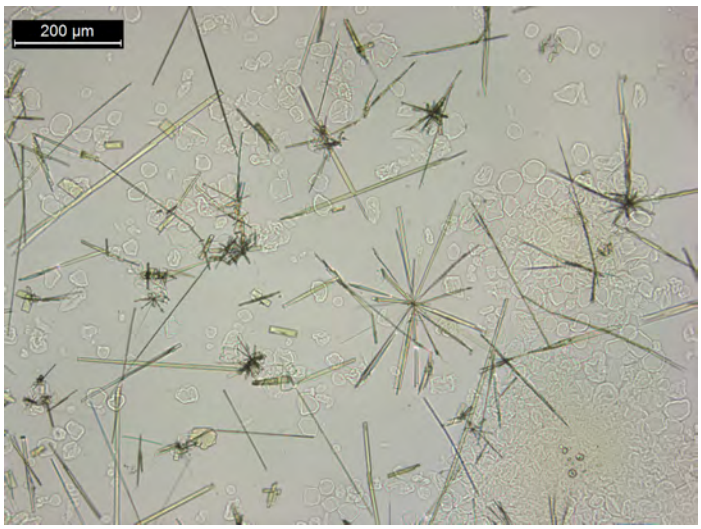

Figure 15. Direct test: One prill from a 10 mg Dexedrine® capsule was crushed and gently stirred with 10 µL of $HAuCl_4$ reagent. Crystals form long yellow rods.

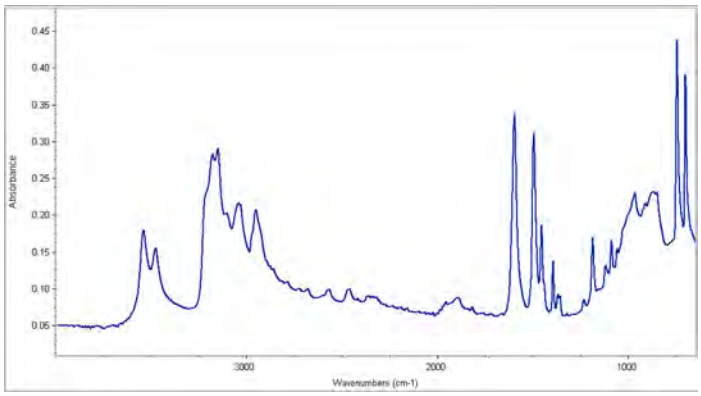

Figure 16. Infrared spectrum of *d*-amphetamine gold chloride precipitate. Download SPC file.

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d-Amphetamine: Platinum Chloride

REAGENT 2: Platinum Chloride (H_2PtCl_6)

1 g $H_2PtCl_6 \cdot 6H_2O$ in (1+3) H_3PO_4, make up to 20 mL. (1+3) H_3PO_4 is dilute phosphoric acid made by combining one part (e.g. 5 mL) of concentrated phosphoric acid with three parts (e.g. 15 mL) of water.

Test Method

There are two test methods: volatility and direct; both give the same crystals.
Volatility test: With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring for 5 minutes. Remove coverslip and place faceup to expose the drop to air. **Direct test:** Dissolve sample in 5 µL of concentrated phosphoric acid, then add 5 µL of reagent.

References

1. ASTM E1969-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.

Limit of Detection

2 PPP for both test methods.

Time Required for Crystal Formation

Volatility: 1–2 minutes
Direct: Immediate

Crystal Morphology and Test Notes

Crystals are colorless needles and rods that sometimes form rosettes of needles and rods. The first crystals that develop are thin, hair-like and often curved, and thicken over time.

Photomicrograph of Typical Crystals

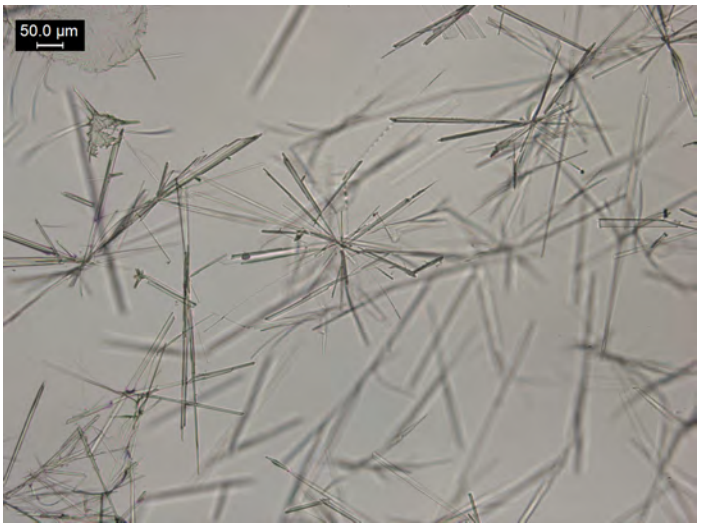


Figure 1. Direct test: 2 PPP *d*-amphetamine dissolved in 2 µL of concentrated H_3PO_4 and 2 µL of H_2PtCl_6 reagent.

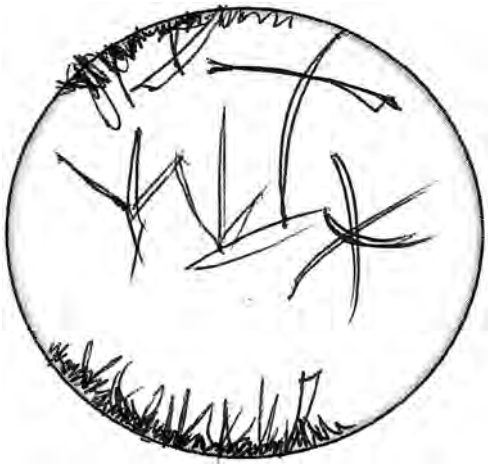
Pharmaceuticals, Adulterants or Other Drug Interactions

This microcrystal test was successful on one crushed prill (≈2 PPP) from a 10 mg capsule and on one crushed prill (≈2 PPP) from 10 mg "XR" extended release formulation.

IR Spectrum

See Figure 10. Download SPC file.

PLM Optical Properties

Approximate Size Range	< 1 µm width, > 1 mm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	1.642–1.700
Morphology Illustration  *not to scale*	
How Crystals Were Dried for RI Measurement	Excess liquid was wicked with lab tissue then washed with chloroform using a tungsten needle. It was difficult to see crystals in closely matching RI liquid due to the narrow width of the needles.
Estimated Birefringence	Low
Extinction	Parallel
Sign of Elongation	Positive (+) and negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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d-Amphetamine: Platinum Chloride (continued)

Figure 2. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of the hanging drop.

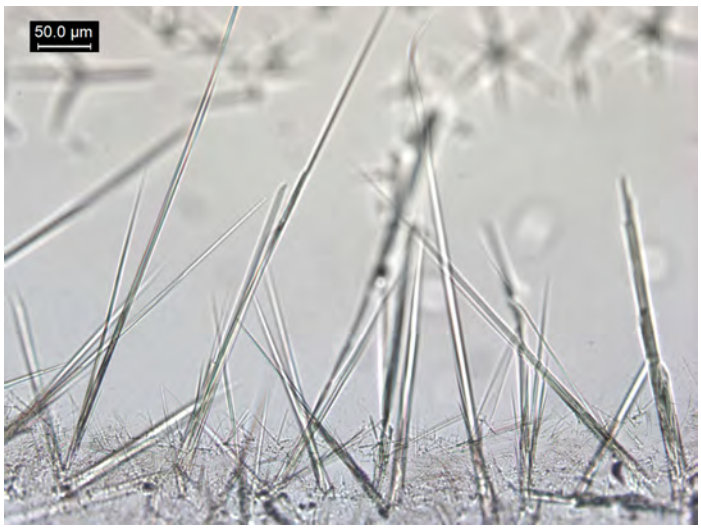

Figure 3. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of the hanging drop.

Figure 4. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of the hanging drop.

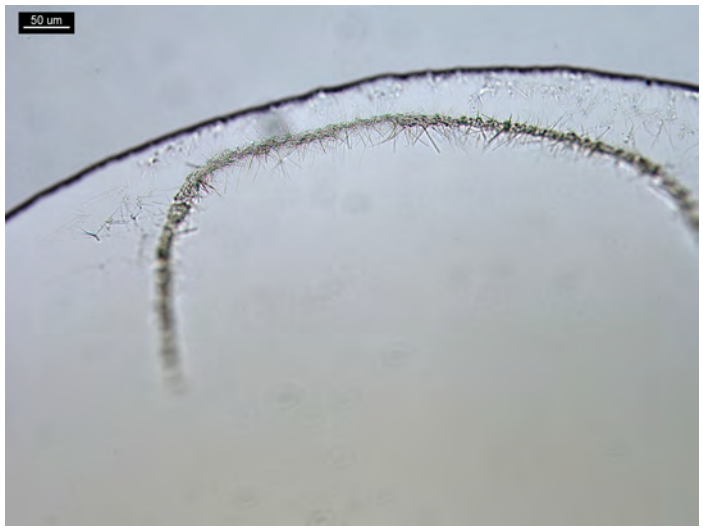

Figure 5. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of a hanging drop. Sometimes the crystals detach and move towards the center of the hanging drop.

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d-Amphetamine: Platinum Chloride (continued)

Figure 6. Volatility test: 2 PPP of *d*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent. For this photomicrograph, the coverslip with the hanging drop was removed from the reaction chamber and placed drop-side down onto the glass slide.

Figure 7. Same as Figure 6. Crystals appear nearly isotropic; crossed polars and Red I compensator.

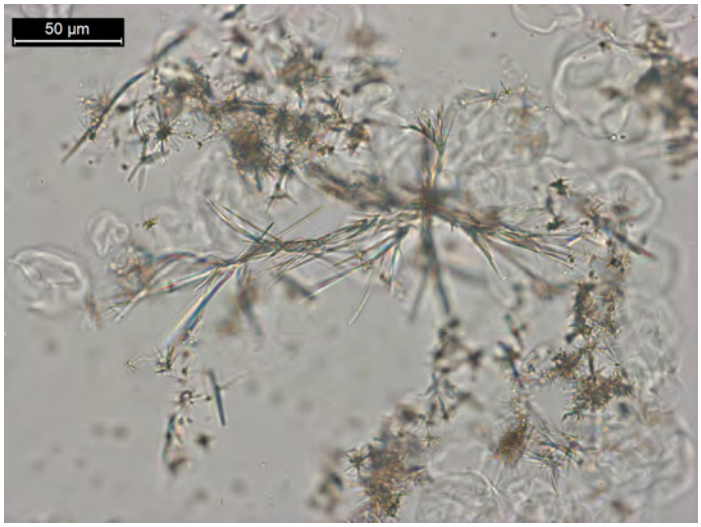

Figure 8. Direct test: One prill from a 10 mg Dexedrine® capsule gently stirred with 10 µL of H_2PtCl_6 reagent.

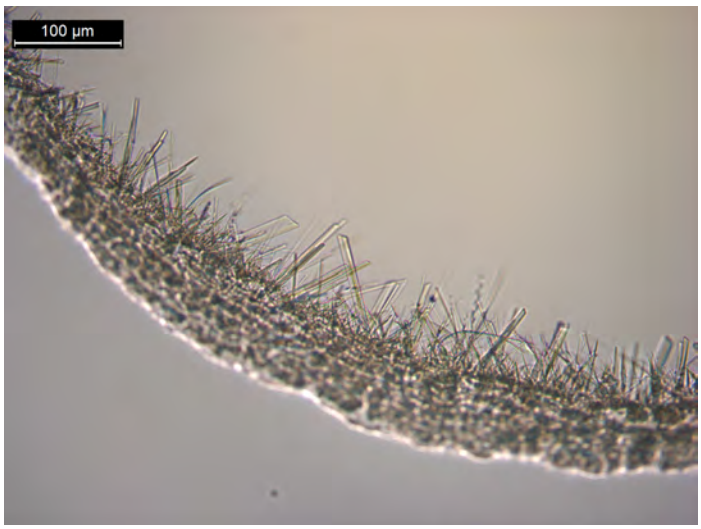

Figure 9. Volatility test: One prill from a 10 mg Dexedrine® capsule and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent.

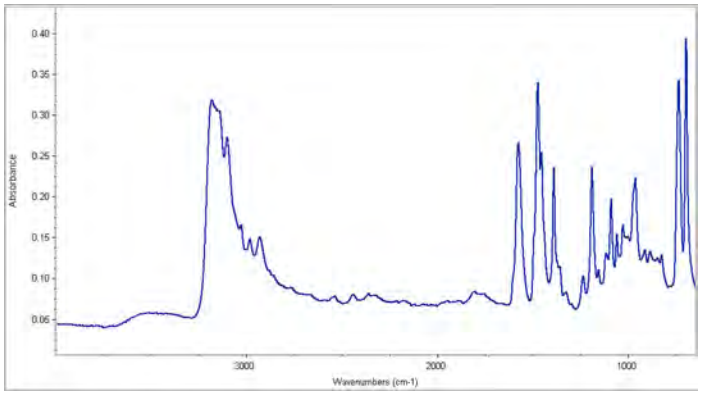

Figure 10. Infrared spectrum of *d*-amphetamine platinum chloride precipitate. Download SPC file.

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dl-Amphetamine: Gold Chloride

REAGENT 1: Gold Chloride ($HAuCl_4$,)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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

There are two test methods, volatility and direct; both give the same crystals.

Volatility test: With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring. After 5 minutes, or longer if oily drops do not form at the edge of the hanging drop, remove coverslip and place faceup to expose hanging drop to air.

Direct test: Dissolve sample in 5 µL concentrated phosphoric acid, then add 5–10 µL of reagent, or add 10 µL of reagent directly to sample; gentle stirring is optional.

References

1. ASTM E1969-11. Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.

Limit of Detection

2 PPP for volatility test, 5–10 PPP for some pharmaceutical tablets, one prill (≈2 PPP) from capsules, and 5 PPP for direct test.

Time Required for Crystal Formation

Volatility: 5 minutes

Direct: Up to 5 minutes (longer if < 5 PPP is used)

Crystal Morphology and Test Notes

Thin, yellow, irregular and serrated plates often appear in star or branched-cluster formations and as nearly perfect square plates with ≈ 90° angles.

Photomicrograph of Typical Crystals

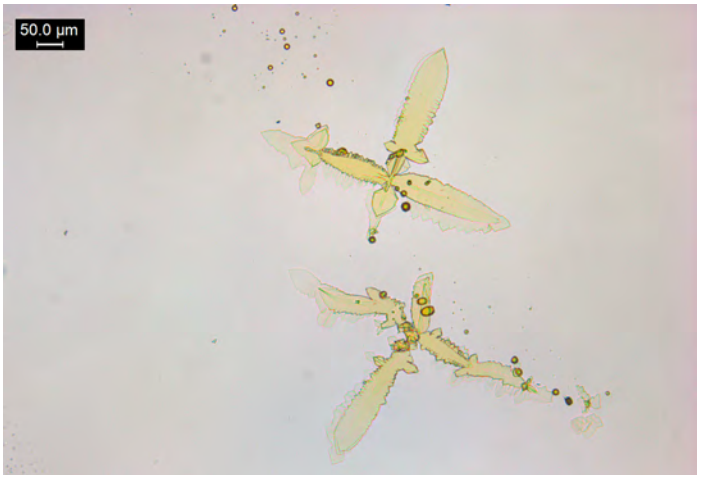

Figure 1. Volatility test: 2 PPP *dl*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of $HAuCl_4$ reagent.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 PPP of crushed 5 mg, 10 mg and 20 mg tablets, and one crushed prill (≈2 PPP) from a 30 mg capsule. If *d*- and *dl*- amphetamine are present together, *d*-amphetamine crystals (rods or segmented rods) are often observed together with *dl*-amphetamine crystals (serrated plates). Note: *dl*- crystals may take a few extra minutes to appear.

IR Spectrum

See Figure 12. Download SPC file.

PLM Optical Properties

Approximate Size Range	10–200 µm. Branched-cluster formations and platy crystals can be > 1 mm.
Color/Pleochroism	Yellow; not pleochroic
Refractive Indices (RI)	All RIs are > 1.700.
Morphology Illustration *not to scale*	
How Crystals Were Dried for RI Measurement	Excess liquid was wicked with lab tissue then crystals were washed with chloroform using a tungsten needle.
Estimated Birefringence	Moderate–High
Extinction	Complete
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Biaxial, negative (–)

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dl-Amphetamine: Gold Chloride (continued)

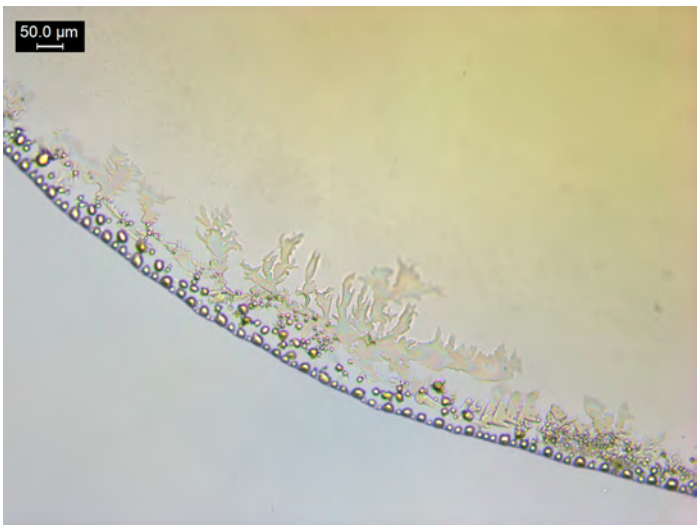

Figure 2. Volatility test: 2 PPP *dl*-amphetamine and one drop of 40% NaOH in a 5 µL hanging drop of $HAuCl_4$ reagent. Oily drops precede crystal formation. Typical crystals begin to form at the edge of the hanging drop.

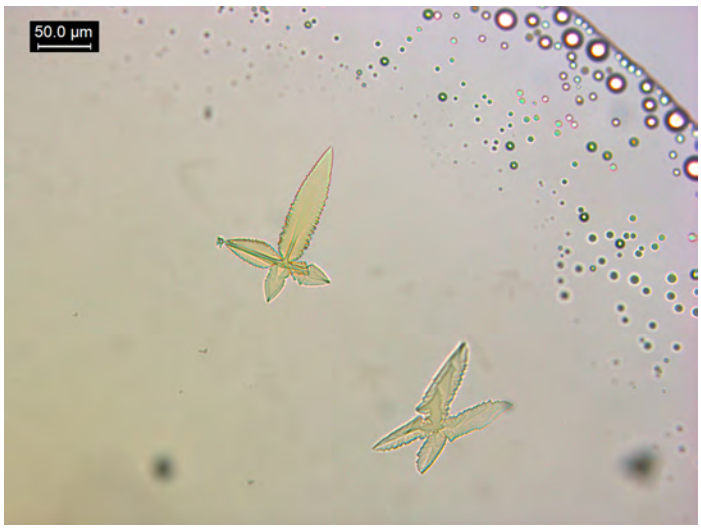

Figure 3. Volatility test: 2 PPP *dl*-amphetamine and one drop of 40% NaOH in a 5 µL hanging drop of $HAuCl_4$ reagent.

Figure 4. Volatility test: 2 PPP *dl*-amphetamine and one drop of 40% NaOH in a 5 µL hanging drop of $HAuCl_4$ reagent, after 5 minutes the coverslip with the hanging drop was removed, inverted faceup and exposed to air. Crystals grow as branched, serrated plates.

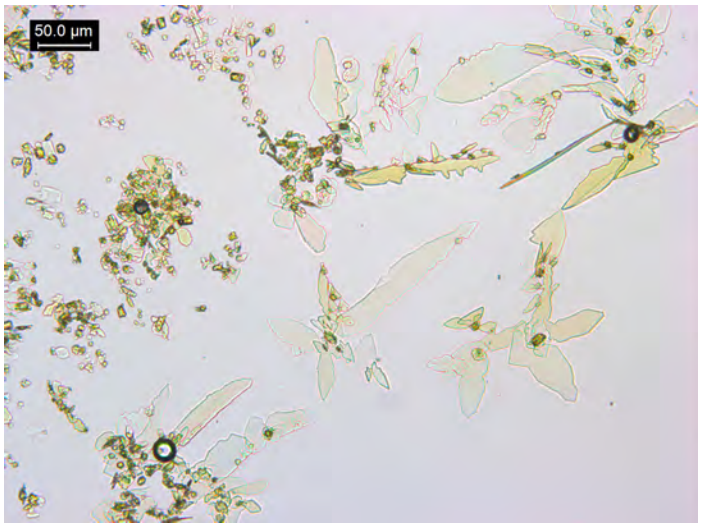

Figure 5. Volatility test: 2 PPP *dl*-amphetamine and one drop of 40% NaOH in a 5 µL hanging drop of $HAuCl_4$ reagent. The coverslip with the hanging drop was placed facedown on the slide to flatten it for this photomicrograph.

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dl-Amphetamine: Gold Chloride (continued)

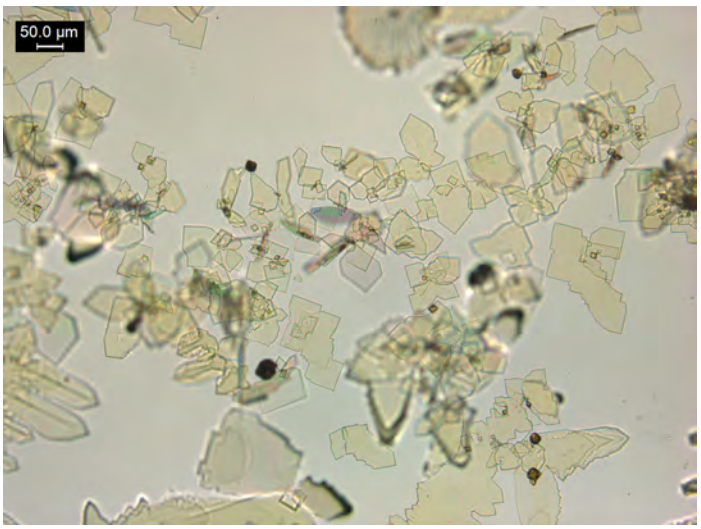

Figure 6. Direct test: 10 µL of the $HAuCl_4$ reagent added to 5 PPP of *dl*-amphetamine. Note the approximate 90° angles and nearly perfect squares.

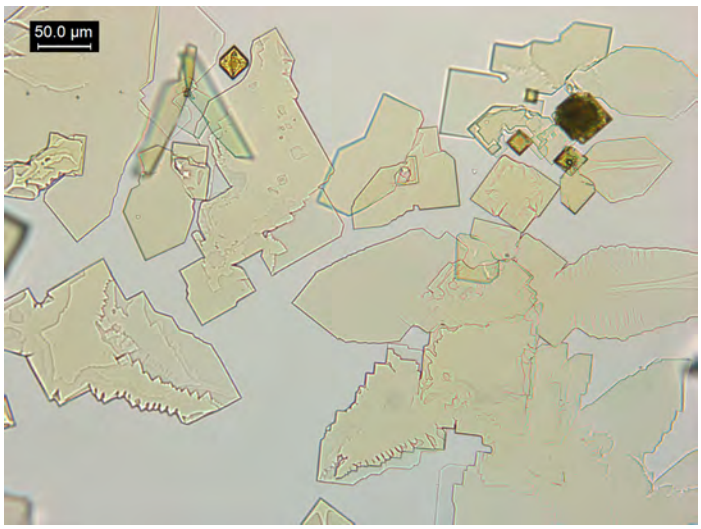

Figure 7. Direct test: 10 µL of the $HAuCl_4$ reagent added to 5 PPP of *dl*-amphetamine. Note the approximate 90° angles and nearly perfect squares.

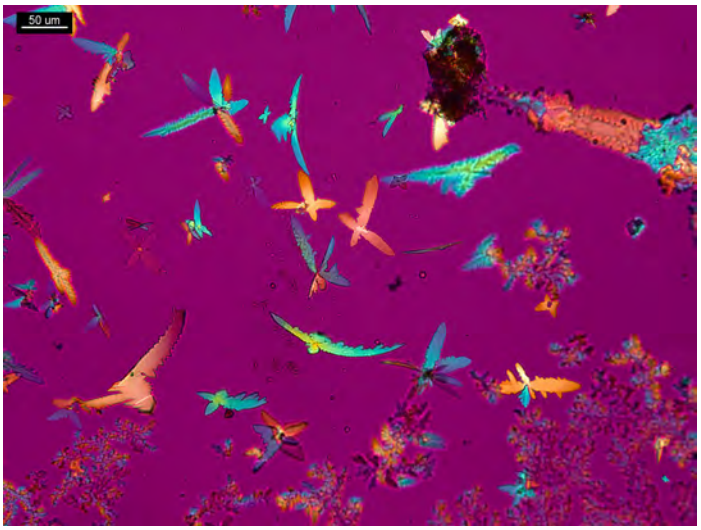

Figure 8. Direct test: One prill from a 10 mg capsule was crushed and gently stirred with 10 µL of $HAuCl_4$ reagent. Crystals are thin plates.

Figure 9. Direct test: 5 PPP from a 10 mg tablet crushed and gently stirred with 10 µL of $HAuCl_4$ reagent. This test detected *d*-amphetamine (long yellow rods, left) and *dl*-amphetamine (serrated plates, upper right).

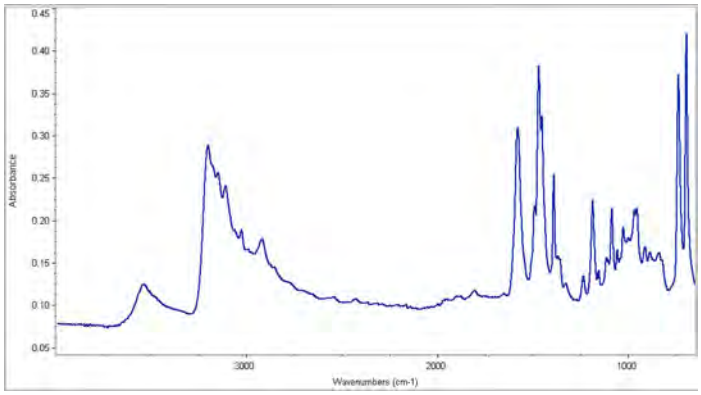

Figure 10. Infrared spectrum of *dl*-amphetamine gold chloride precipitate. Download SPC file.

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dl-Amphetamine: Platinum Chloride

REAGENT 2: Platinum Chloride (H_2PtCl_6)

1 g $H_2PtCl_6 \cdot 6H_2O$ in (1+3) H_3PO_4, make up to 20 mL. (1+3) H_3PO_4 is dilute phosphoric acid made by combining one part (e.g. 5 mL) of concentrated phosphoric acid with three parts (e.g. 15 mL) of water.

Test Method

There are two test methods, volatility and direct; both give the same crystals.
Volatility test: With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring for 5 minutes. Remove coverslip and place faceup to expose drop to air. **Direct test:** Dissolve sample in 5 µL of concentrated phosphoric acid, then add 5 µL of reagent.

References

1. ASTM E1969-11. Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.

Limit of Detection

2 PPP for both test methods (6 PPP for most pharmaceutical tablets and capsules)

Time Required for Crystal Formation

Volatility: 1–10 minutes
Direct: Up to 10 minutes

Crystal Morphology and Test Notes

Crystals are colorless blades and rods, which sometimes form rosettes. The first crystals that develop are thin, hair-like and often curved, becoming wider over time.

Photomicrograph of Typical Crystals

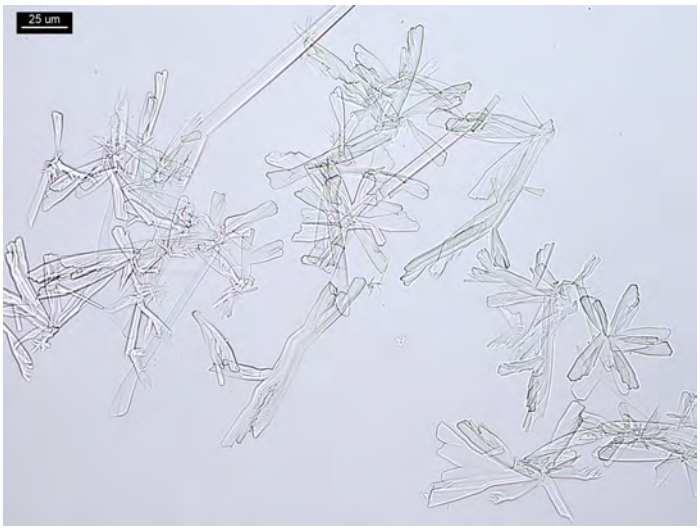


Figure 1. Volatility test: 3 PPP *dl*-amphetamine and one drop of 40% NaOH; crystals in a 5 µL hanging drop of H_2PtCl_6 reagent.

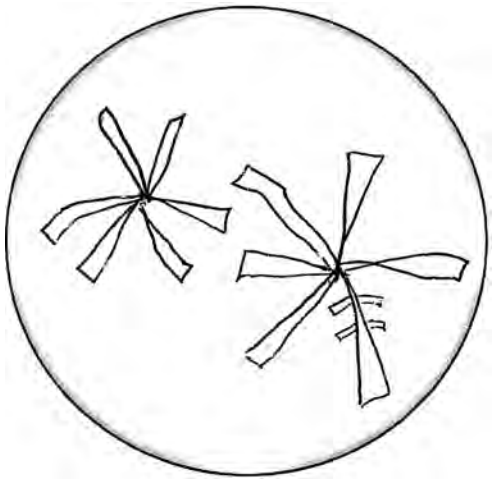
Pharmaceuticals, Adulterants or Other Drug Interactions

Platinum chloride forms crystals faster than gold chloride but is not as sensitive. The volatility test is preferred for tablets and capsules because the direct test often results in poorly formed crystals in the presence of significant amounts of pharmaceutical fillers. Tests were successful on 6 PPP from a crushed 5 mg, 10 mg and 20 mg tablets, and on three crushed prills (≈6 PPP) from a 30 mg capsule.

PLM Optical Properties

Approximate Size Range	10–100 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	1.642–1.700

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked with lab tissue then washed with chloroform using a tungsten needle.
Estimated Birefringence	Very low (nearly isotropic)
Extinction	Parallel, undulose and polycrystalline
Sign of Elongation	Positive (+) and negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 12. Download SPC file.

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dl-Amphetamine: Platinum Chloride (continued)

Figure 2. Direct test: 2 PPP *dl*-amphetamine dissolved in 5 µL of concentrated H_3PO_4 and 5 µL of H_2PtCl_6 reagent.

Figure 3. Direct test: 2 PPP *dl*-amphetamine dissolved in 5 µL of concentrated H_3PO_4 and 5 µL of H_2PtCl_6 reagent.

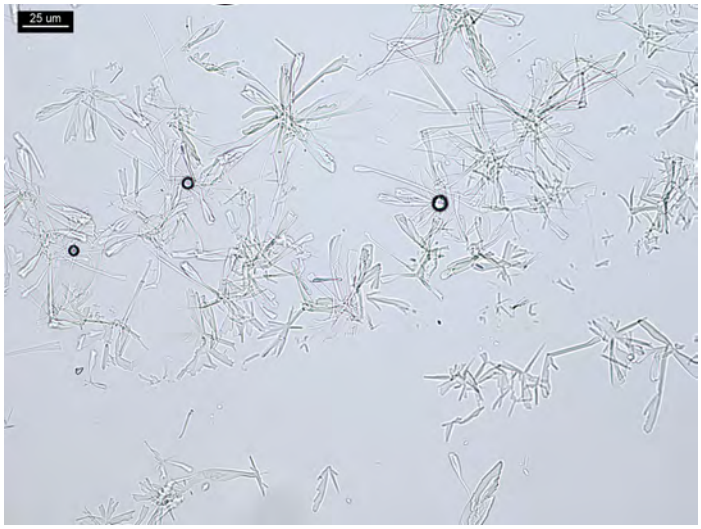

Figure 4. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent for 5 minutes. Then, the coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide.

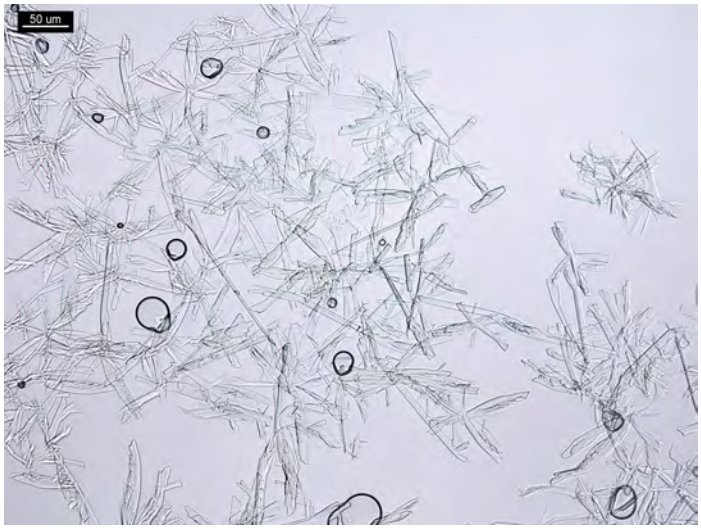

Figure 5. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent for 5 minutes. Then, the coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide.

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dl-Amphetamine: Platinum Chloride (continued)

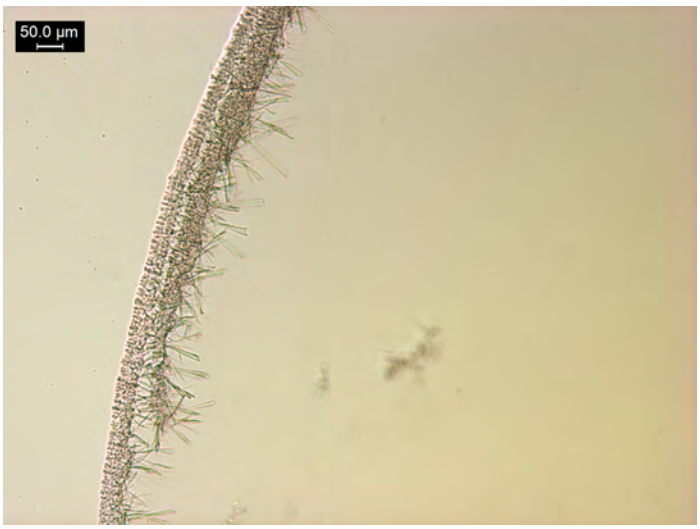

Figure 6. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of the hanging drop.

Figure 7. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals grow from a crust that forms at the edge of the hanging drop. The coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide.

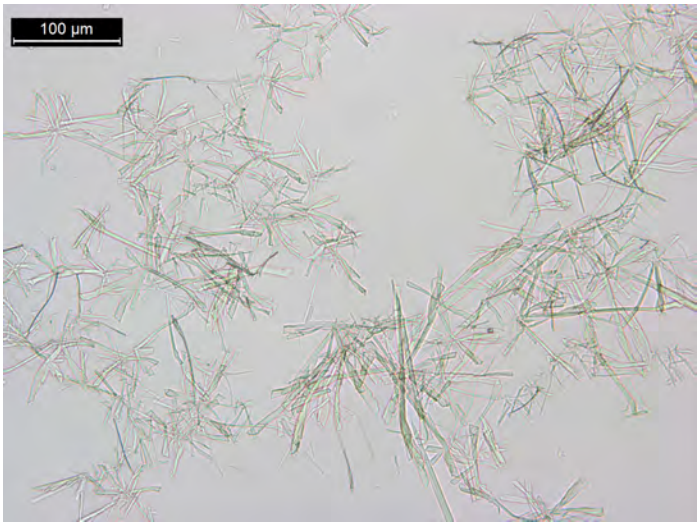

Figure 8. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent for 5 minutes. The coverslip with the hanging drop was removed from the reaction chamber and placed face-down onto the glass slide.

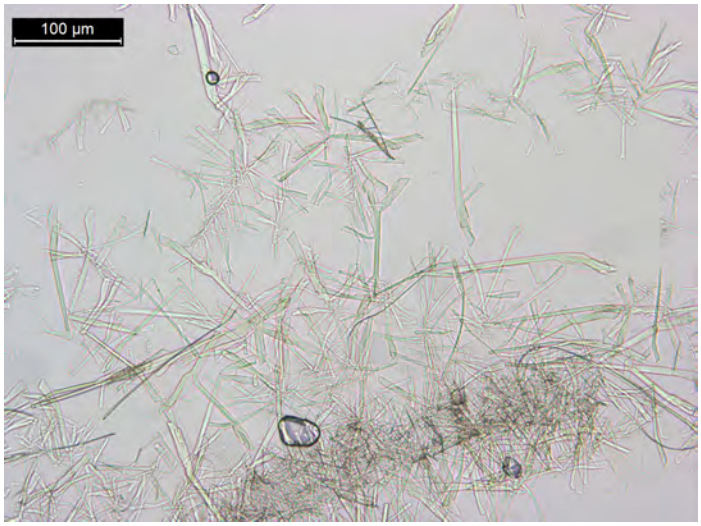

Figure 9. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent for 5 minutes. The coverslip with the hanging drop was removed from the reaction chamber and placed face-down onto the glass slide.

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dl-Amphetamine: Platinum Chloride (continued)

Figure 10. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent. Crystals have very low birefringence; crossed polars and Red I compensator.

Figure 11. Volatility test: One drop of 40% NaOH added to 3 PPP of *dl*-amphetamine. Crystals formed in a 5 µL hanging drop of H_2PtCl_6 reagent; crossed polars and Red I compensator.

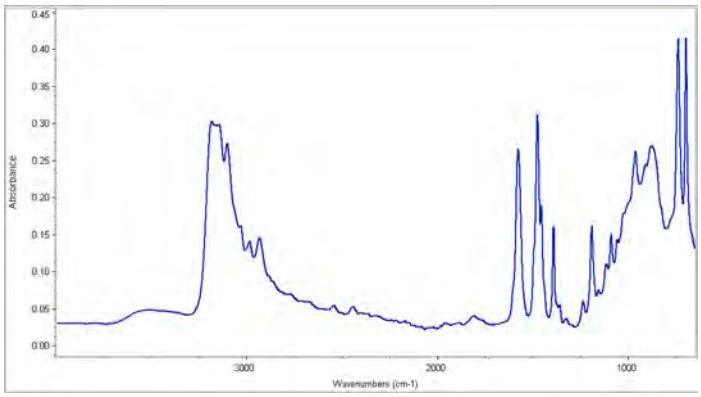

Figure 12. Infrared spectrum of *dl*-amphetamine platinum chloride precipitate. Download SPC file.

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1-Benzylpiperazine

REAGENT 1: Platinum Bromide (H_2PtBr_6)

5% aqueous: 5 g H_2PtBr_6 in H_2O, make up to 100 mL

Test Method

Direct test: Dissolve sample in 5 µL of water, then add 5 µL of reagent. The reagent is placed on a coverslip, which is then inverted and dropped onto the sample.

References

1. Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) Benzylpiperazine (BZP) Monograph, http://swgdrug.org/Monographs/BENZYLPIPERAZINE.pdf (accessed October 2015). Note: The SWGDRUG monograph does not clearly reference a reagent recipe. The recipe included in this monograph is from a personal communication with a DEA drug chemist.

Limit of Detection

1 PPP or less

Time Required for Crystal Formation

Rectangular and square plates after ≈ 1 minute

Crystal Morphology and Test Notes

Crystals form yellow rectangular and square plates with ≈ 90° interfacial angles. Most lay flat or sometimes on edge. Serrated X-shaped plates are also formed.

Photomicrograph of Typical Crystals

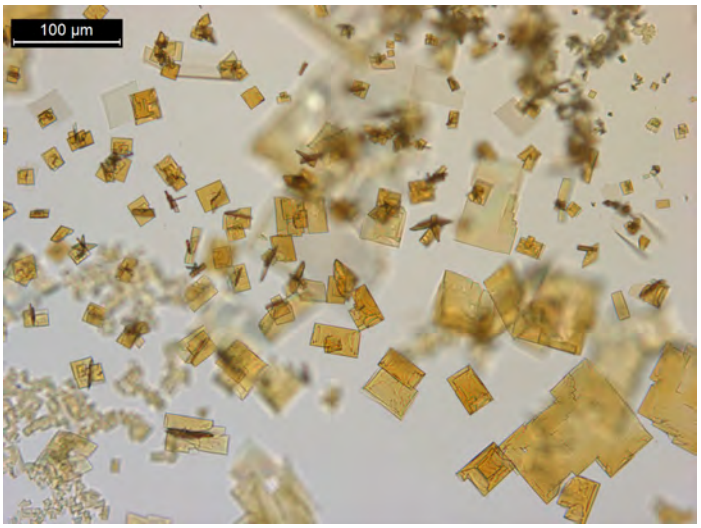


Figure 1. 1 PPP of BZP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form yellow rectangular and square plates.

Pharmaceuticals, Adulterants or Other Drug Interactions

Trifluoromethylphenylpiperazine (TFMPP) may be mixed with BZP in homemade tablets. In 1:1 and 5:1 ratios (BZP:TFMPP), TFMPP had little or no effect on BZP crystal formation. In 1:5 ratios (BZP:TFMPP), some distorted crystals were seen, including rectangles with indented ends; some typical square and rectangular BZP crystals were also evident.

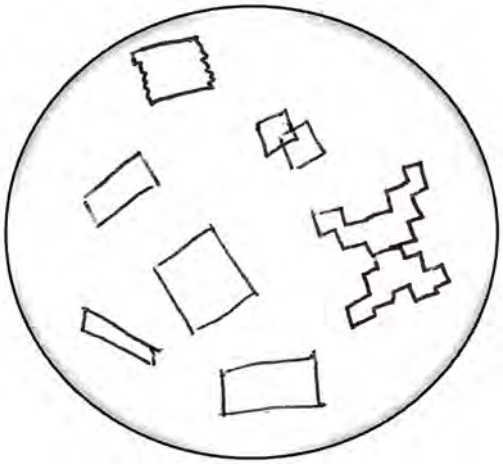
IR Spectrum

See Figure 16. Download SPC file.

PLM Optical Properties

Approximate Size Range	20–30 µm
Color/Pleochroism	Yellow; not pleochroic
Refractive Indices (RI)	n > 1.700

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature.
Estimated Birefringence	Very low (nearly isotropic)
Extinction	Parallel; some dispersed extinction
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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1-Benzylpiperazine (BZP): Platinum Bromide (continued)

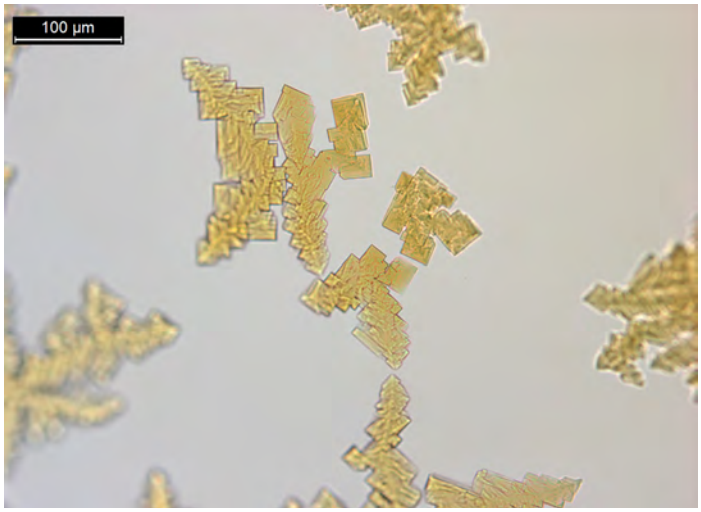

Figure 2. 1 PPP of BZP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates.

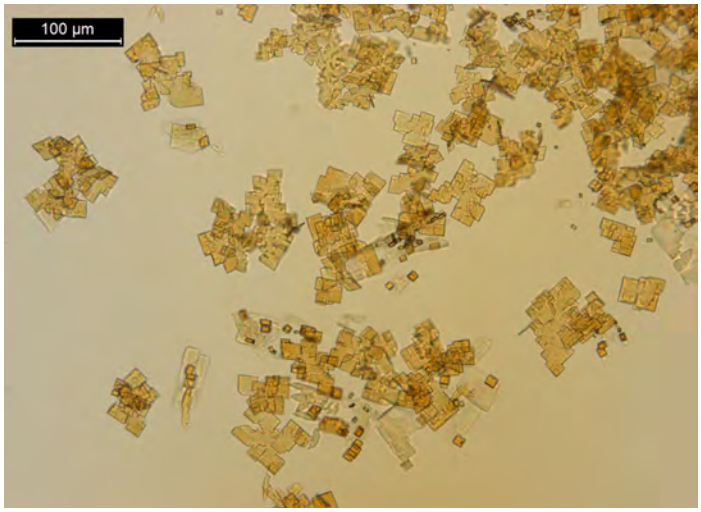

Figure 3. 1 PPP of BZP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates.

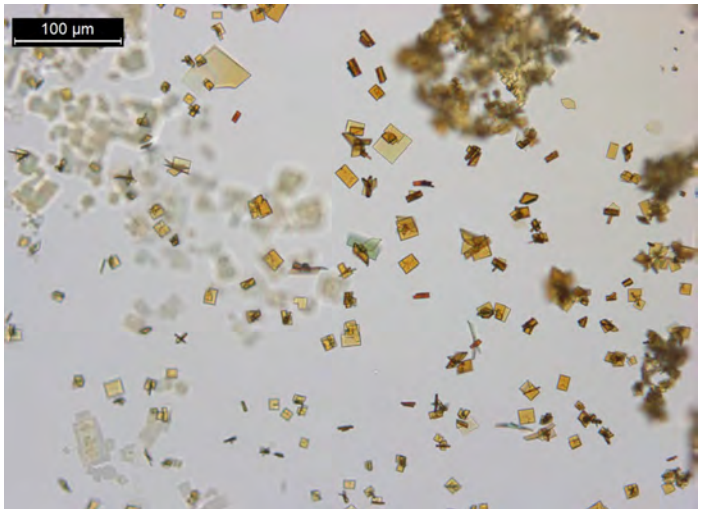

Figure 4. 1 PPP of BZP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates; some are lying on edge.

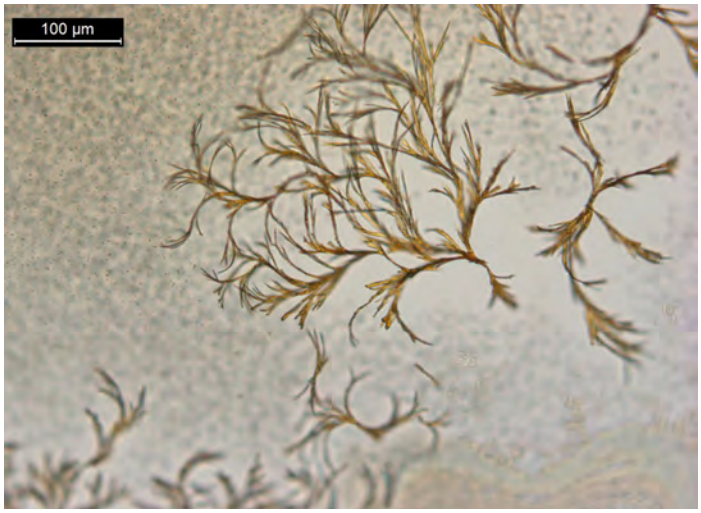

Figure 5. TFMPP only (no BZP) dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form wispy, dendritic feathers.

Figure 6. TFMPP only (no BZP) dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular laths and dendrites.

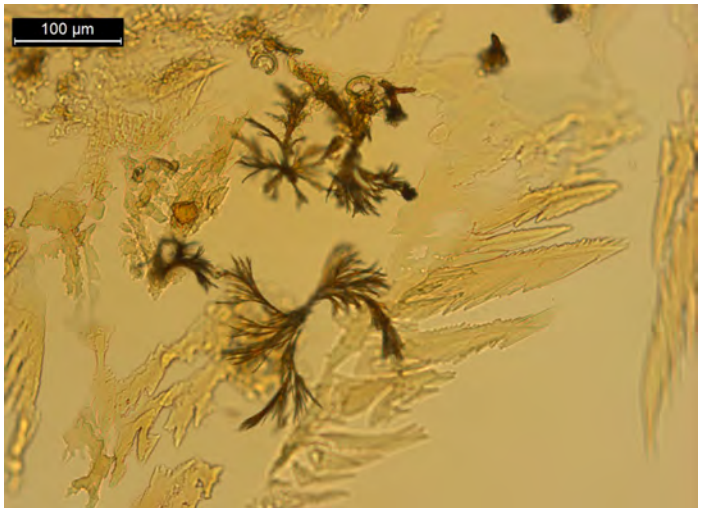

Figure 7. TFMPP only (no BZP) dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form serrated rectangular laths and dendrites.

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1-Benzylpiperazine (BZP): Platinum Bromide (continued)

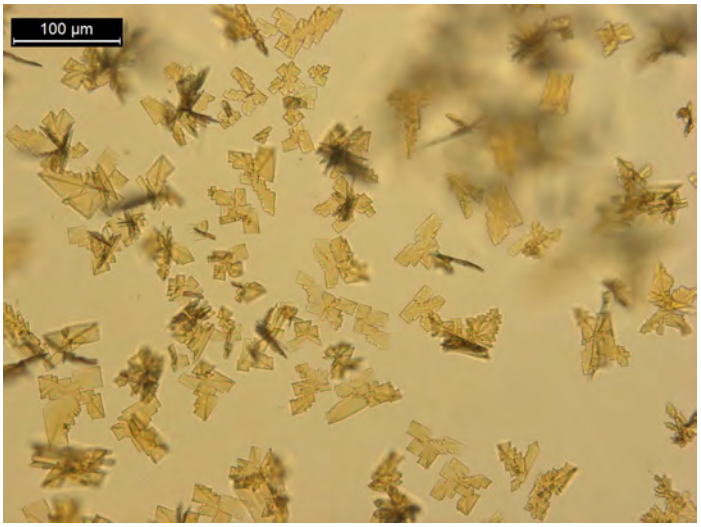

Figure 8. 1 PPP of BZP and 1 PPP TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates, with some serrated X-shaped plates.

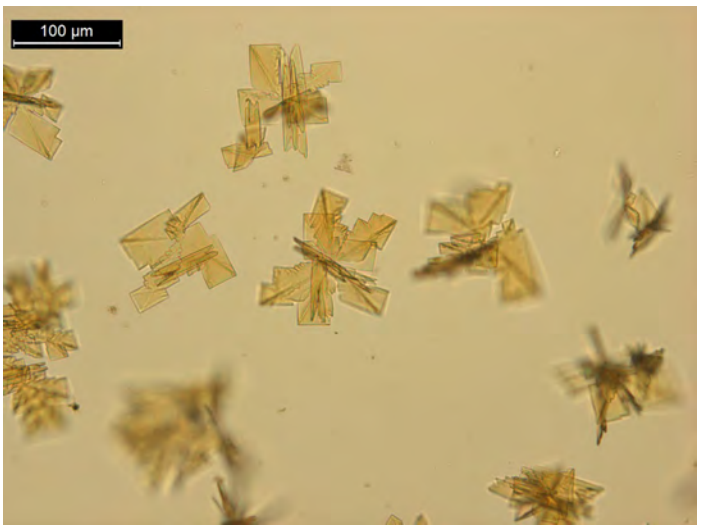

Figure 9. 1 PPP of BZP and 1 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates.

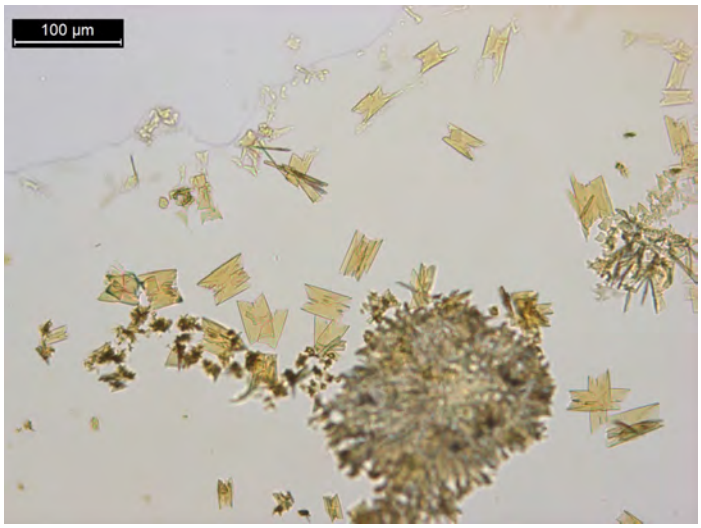

Figure 10. 1 of PPP BZP and 5 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular plates and some distorted crystals with indented ends.

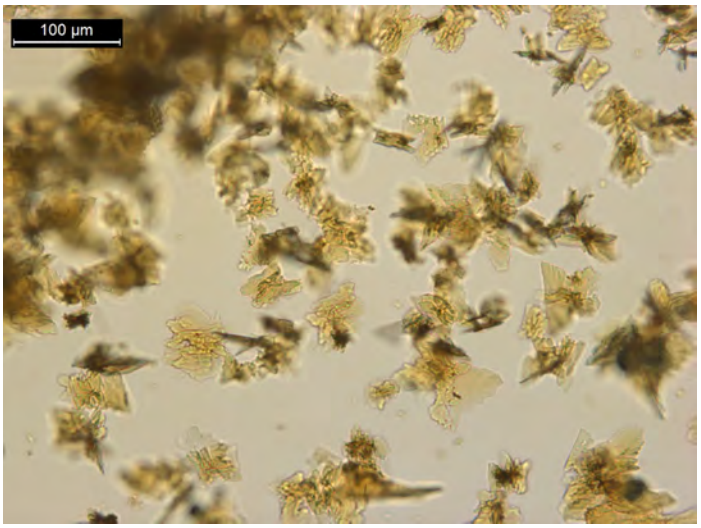

Figure 11. 1 PPP of BZP and 5 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates with distortions.

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1-Benzylpiperazine (BZP): Platinum Bromide (continued)

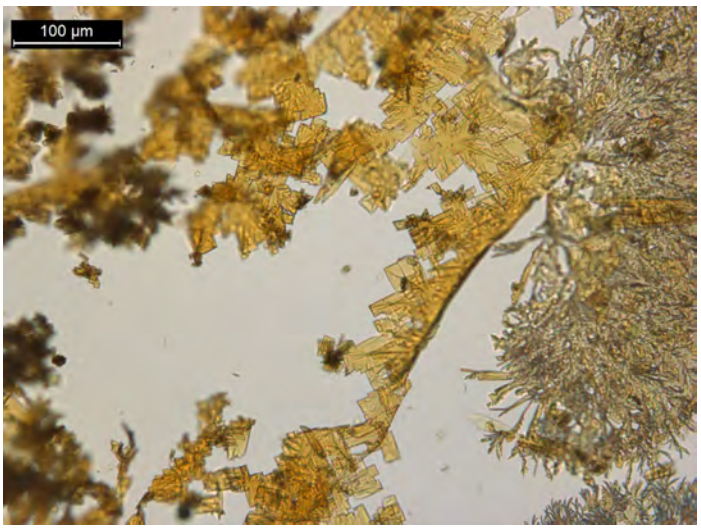

Figure 12. 1 PPP of BZP and 5 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates with distortions.

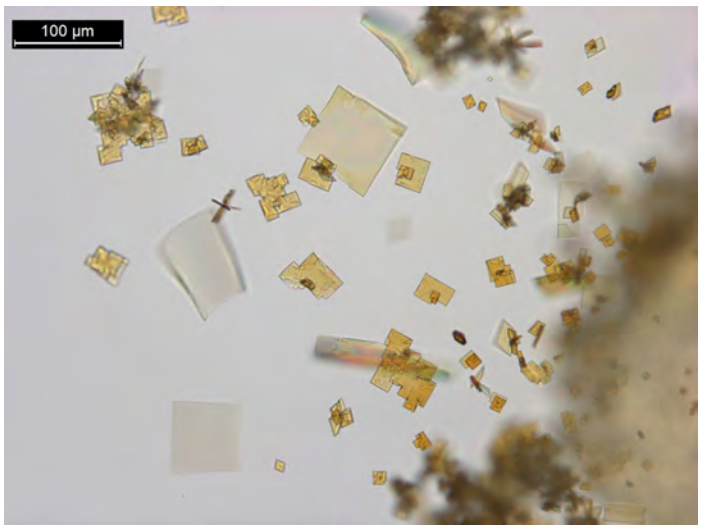

Figure 13. 5 PPP of BZP and 1 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates.

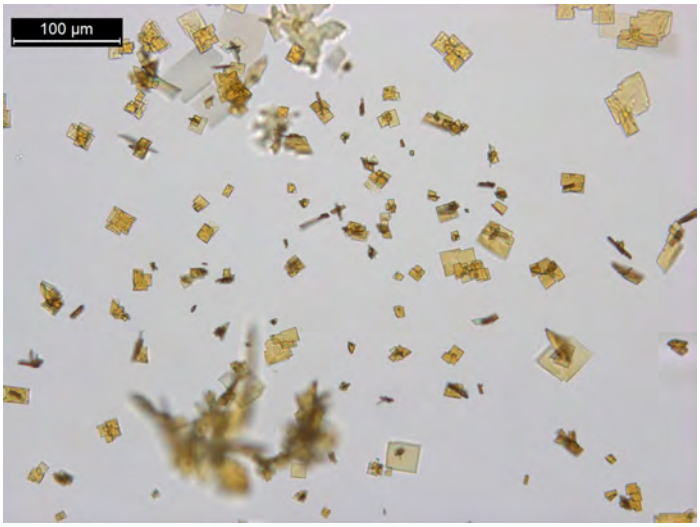

Figure 14. 5 PPP of BZP and 1 PPP of TFMPP dissolved in 5 µL of H_2O and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular and square plates; some are lying on edge.

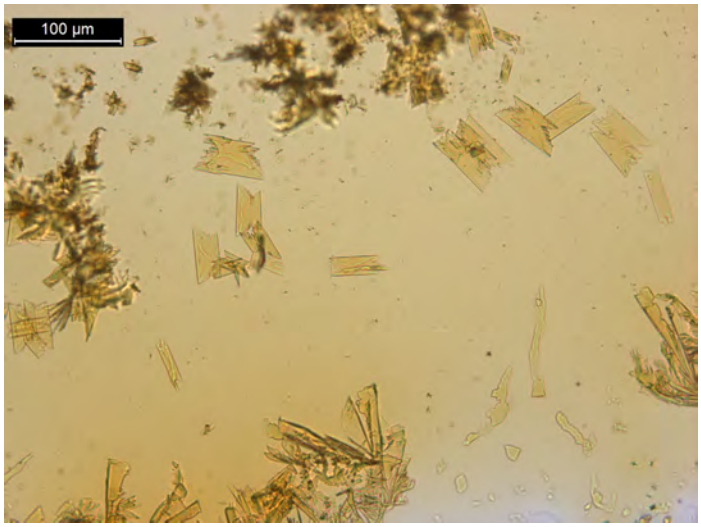

Figure 15. 1 PPP of BZP and 5 µL of a 2.2 mg/mL solution of TFMPP and 5 µL of H_2PtBr_6 reagent. Crystals form rectangular plates and some distorted crystals with indented ends.

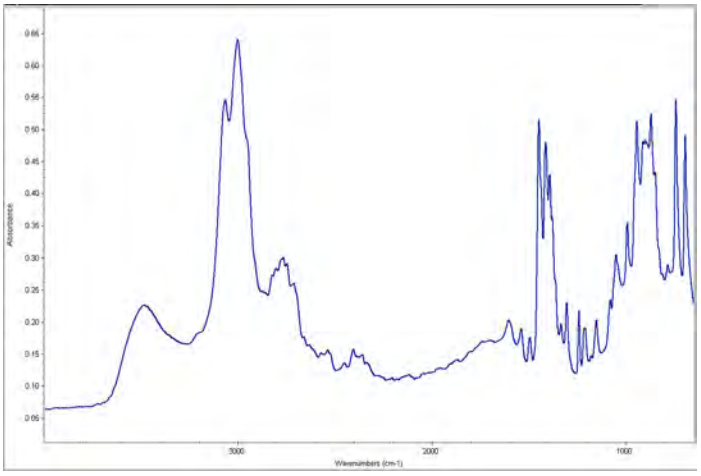

Figure 16. Infrared spectrum of BZP platinum chloride precipitate. Download SPC file.

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Clonazepam: Platinum Chloride

REAGENT: Platinum Chloride (H_2PtCl_6)

10% aqueous: 1g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 10 mL

Test Method

Direct test: Dissolve sample in 5 µL of acetone, then quickly add 5–10 µL of reagent, with or without a coverslip.

References

1. Silletti, D. "Development of a Microcrystal Test for the Detection of Clonazepam," *The Microscope*, 63:2, pp 51–56, 2015.

Limit of Detection

1 PPP (5 PPP for pharmaceutical tablets)

Time Required for Crystal Formation

< 5 minutes

Crystal Morphology and Test Notes

Narrow blades and rods, usually with tapered, pointy ends. Some with blunt or forked ends; often arranged as fans and rosettes.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of clonazepam with 5–10 µL of H_2PtCl_6 reagent. Crystals form narrow blades and rods, sometimes arranged as rosettes.

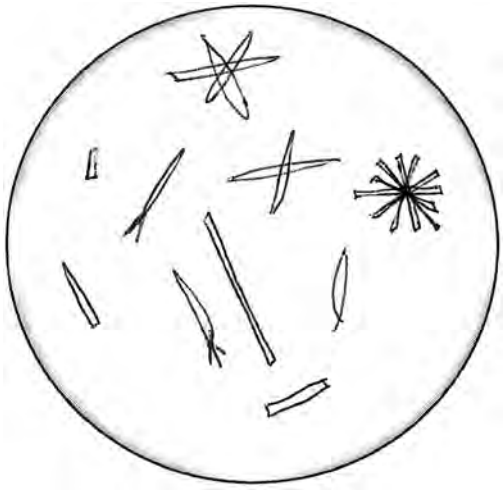
Pharmaceuticals, Adulterants or Other Drug Interactions

Tests were successful on tablets with the following doses of clonazepam: 2 mg, 1 mg and 0.5 mg, and 0.25 mg orally disintegrating tablets. (A coverslip with gentle pressure applied may be used to break up a tablet.)

IR Spectrum

Not available

PLM Optical Properties

Approximate Size Range	1–10 µm width; 10–300 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel > 1.700 n-perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature without a coverslip. Gentle heating resulted in distorted crystals and recrystallized reagent.
Estimated Birefringence	Moderate–High
Extinction	Parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Clonazepam: Platinum Chloride (continued)

Figure 2. 1 PPP of clonazepam with 5–10 µL of H_2PtCl_6 reagent.

Figure 3. 1 PPP of clonazepam with 5–10 µL of H_2PtCl_6 reagent; crossed polars and Red I compensator.

Figure 4. 1 PPP of clonazepam with 5–10 µL of H_2PtCl_6 reagent.

Figure 5. 1 PPP of clonazepam with 5–10 µL of H_2PtCl_6 reagent; crossed polars and Red I compensator.

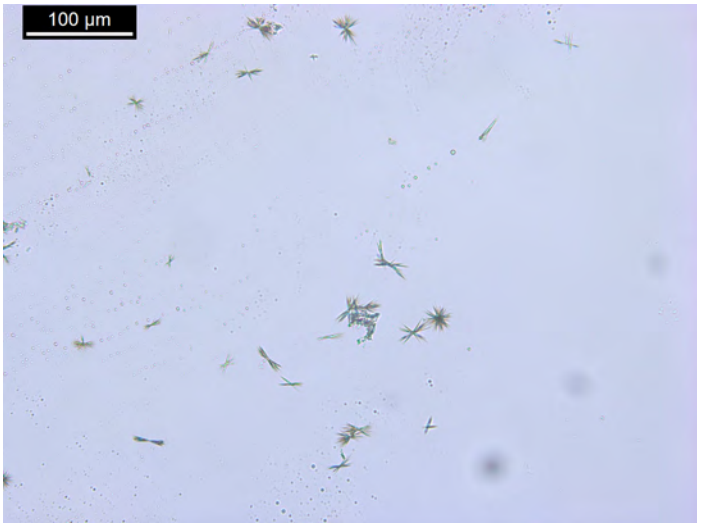

Figure 6. 5 PPP of clonazepam from a 0.25 mg orally disintegrating tablet with 5–10 µL of H_2PtCl_6 reagent. Narrow blades are arranged as rosettes.

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Cocaine: Gold Chloride with Acetic Acid

REAGENT 1A: Gold Chloride ($HAuCl_4$) with Acetic Acid (HOAc)

5% aqueous: 1 g $HAuCl_4 \cdot 3H_2O$ in H_2O, make up to 20 mL

Test Method

Direct test: Dissolve sample in 5 µL of 10% HOAc, then add 5 µL of reagent to the edge of the sample drop; no coverslip. This test method with acetic acid is preferred over hydrochloric acid because the crystals have a more typical morphology and optical properties that are easier to measure.

Reference

1. ASTM E1968-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Cocaine, ASTM International, 2011.

Limit of Detection

1 PPP

Time Required for Crystal Formation

< 1 minute; typical crystals in 2–5 minutes

Crystal Morphology and Test Notes

X-shaped crystals bisected by a barbed rod, comb-like crosses (with ≈ 90° angles and parallel extinction) and individual combs, with some variation in each preparation.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of cocaine in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form X-shapes bisected by a barbed rod; crossed polars and Red I compensator.

Pharmaceuticals, Adulterants or Other Drug Interactions

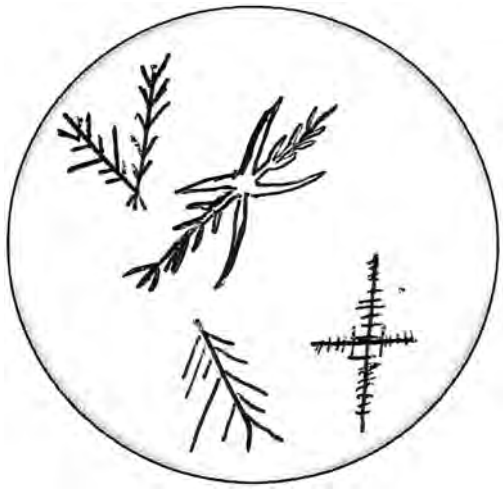
Common adulterants with cocaine that may inhibit or distort crystal formation include caffeine, levamisol, lidocaine, procaine and strychnine. The detectability of cocaine with selected adulterants is listed below:

- Caffeine:cocaine – detectable at 1:5; undetectable at 1:1 and 5:1
- Hydroxyzine:cocaine – detectable at 1:5, 1:1 and 5:1
- Levamisol:cocaine – detectable at 1:5; undetectable at 1:1 and 5:1
- Lidocaine:cocaine – undetectable at 1:5, 1:1 and 5:1
- Phenacetin:cocaine – detectable at 1:5, 1:1 and 5:1
- Procaine:cocaine – undetectable at 1:5, 1:1 and 5:1
- Strychnine:cocaine – undetectable at 1:5, 1:1 and 5:1

PLM Optical Properties

Approximate Size Range	Spine rods ≤ 5 µm width; > 100 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	$n_1 \approx 1.660$ and $n_2 > 1.700$ 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 filter paper.
Estimated Birefringence	High
Extinction	Mostly parallel; some oblique
Sign of Elongation	Positive (+) and negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 10. Download SPC file.

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Cocaine: Gold Chloride with Acetic Acid (continued)

Figure 2. 3 PPP of cocaine in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form combs and crosses; crossed polars and Red I compensator.

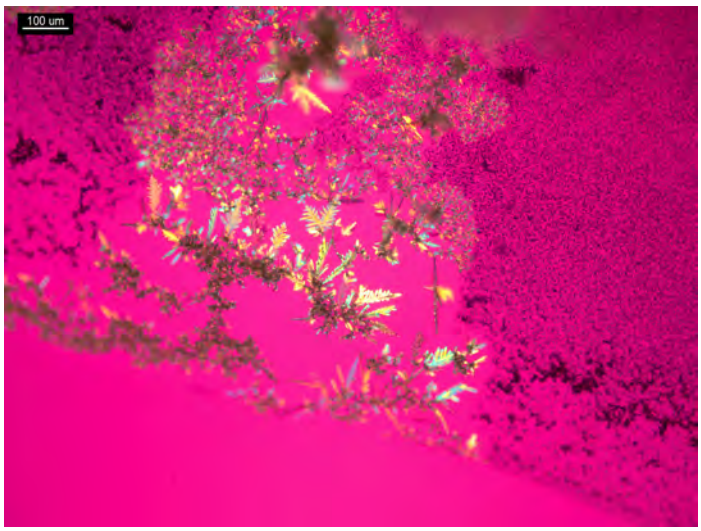

Figure 3. 1 PPP of cocaine in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form combs; crossed polars and Red I compensator.

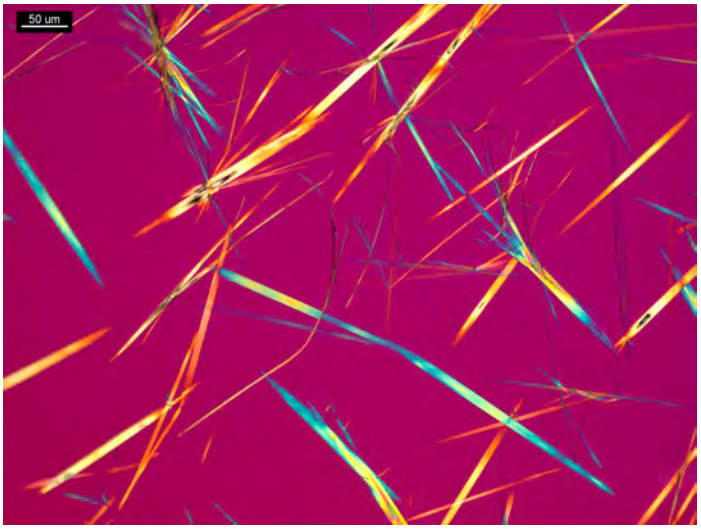

Figure 4. 1 PPP of caffeine (no cocaine) in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form blades; crossed polars and Red I compensator.

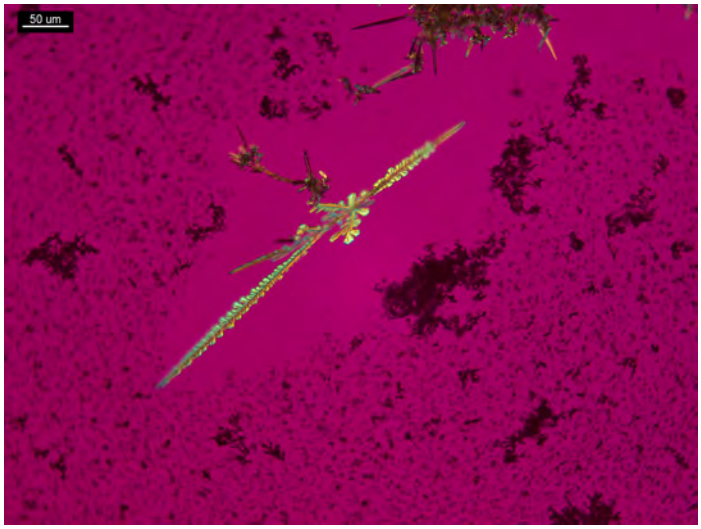

Figure 5. Caffeine:cocaine, 1:5 in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. X-shaped crystals bisected by a barbed rod; crossed polars and Red I compensator.

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Cocaine: Gold Chloride with Acetic Acid (continued)

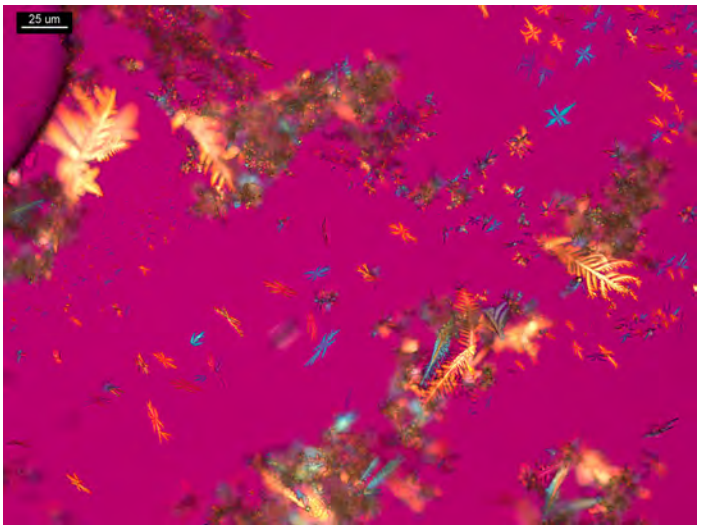

Figure 6. Hydroxyzine:cocaine, 5:1 in 5 µL of 10% HOAc and 5 µL $HAuCl_4$. X-shaped crystals bisected by a barbed rod; crossed polars and Red I compensator.

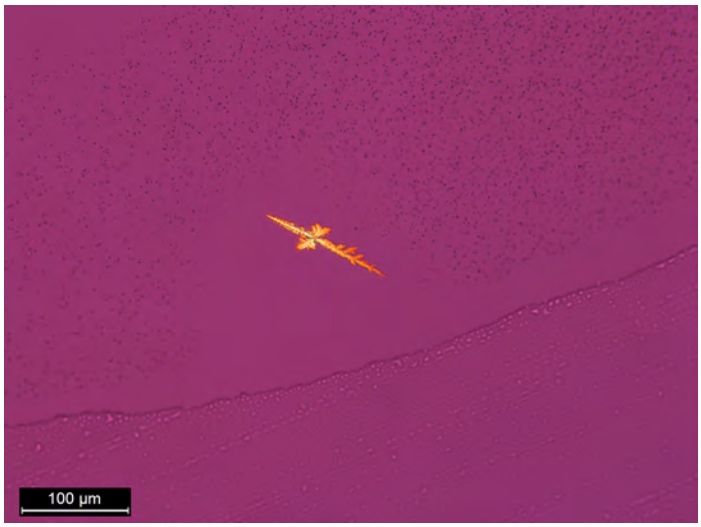

Figure 7. Levamisol:cocaine, 1:5 in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. X-shaped crystals bisected by a barbed rod; crossed polars and Red I compensator.

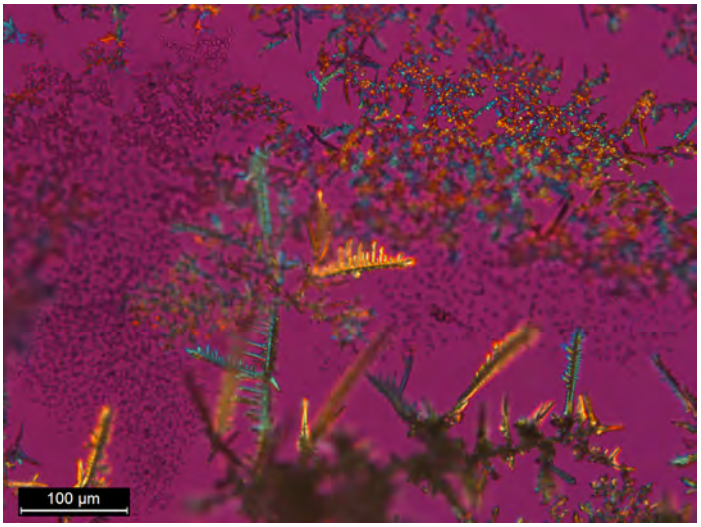

Figure 8. Levamisol:cocaine, 1:5 in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form combs; crossed polars and Red I compensator.

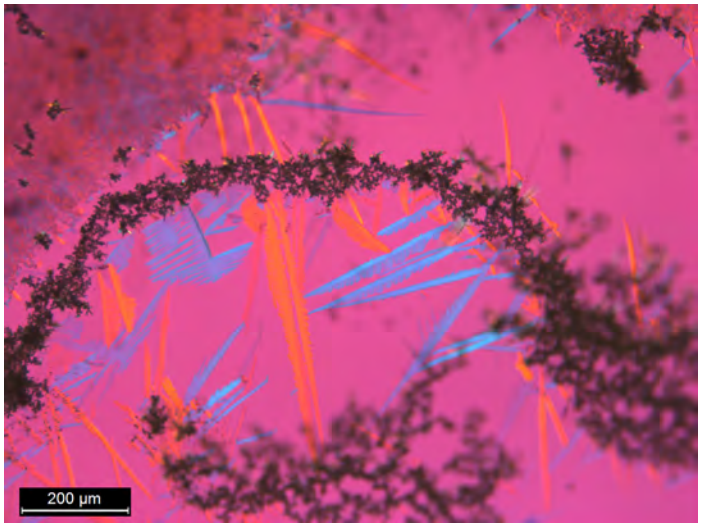

Figure 9. Phenacetin:cocaine, 5:1 in 5 µL of 10% HOAc and 5 µL of $HAuCl_4$ reagent. Crystals form combs; crossed polars and Red I compensator.

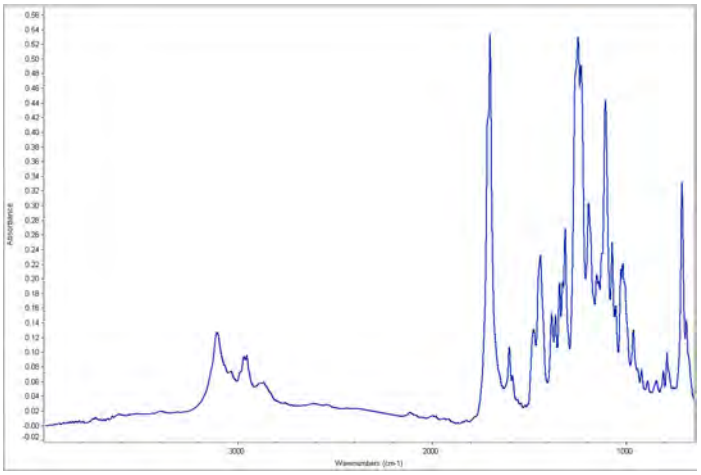

Figure 10. Infrared spectrum of cocaine gold chloride in acetic acid precipitate. Download SPC file.

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Cocaine: Gold Chloride with Hydrochloric Acid

REAGENT 1B: Gold Chloride ($HAuCL_4$) with Hydrochloric Acid (HCl)

5% aqueous: 1 g $HAuCl_4 \cdot 3H_2O$ in H_2O, make up to 20 mL

Test Method

Direct test: Dissolve sample in 5 µL of 10% HCl, then add 5 µL of reagent to the edge of the sample drop; no coverslip.

Reference

1. ASTM E1968-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Cocaine, ASTM International, 2011.

Limit of Detection

1 PPP

Time Required for Crystal Formation

2–5 minutes

Crystal Morphology and Test Notes

Comb-like crosses, individual combs and clusters of rods.

Photomicrograph of Typical Crystals

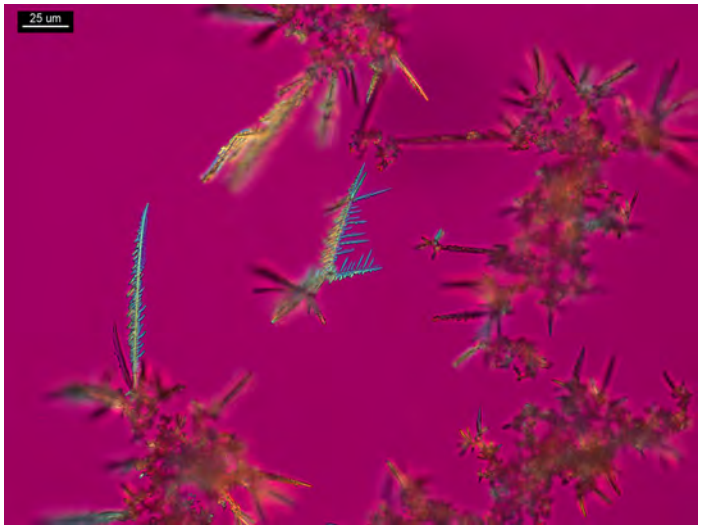


Figure 1. 1 PPP of cocaine in 5 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent. Crystals form combs; crossed polars and Red I compensator.

Pharmaceuticals, Adulterants or Other Drug Interactions

Common adulterants with cocaine that may inhibit or distort crystal formation include caffeine, levamisol, lidocaine, procaine and strychnine. The detectability of cocaine with selected adulterants is listed below:

- Caffeine:cocaine – detectable at 1:5; undetectable at 1:1 and 5:1
- Hydroxyzine:cocaine – detectable at 1:5, 1:1 and 5:1
- Levamisol:cocaine – detectable at 1:5; undetectable at 1:1 and 5:1
- Lidocaine:cocaine – undetectable at 1:5, 1:1 and 5:1
- Phenacetin:cocaine – detectable at 1:5, 1:1 and 5:1
- Procaine:cocaine – undetectable at 1:5, 1:1 and 5:1
- Strychnine:cocaine – undetectable at 1:5, 1:1 and 5:1

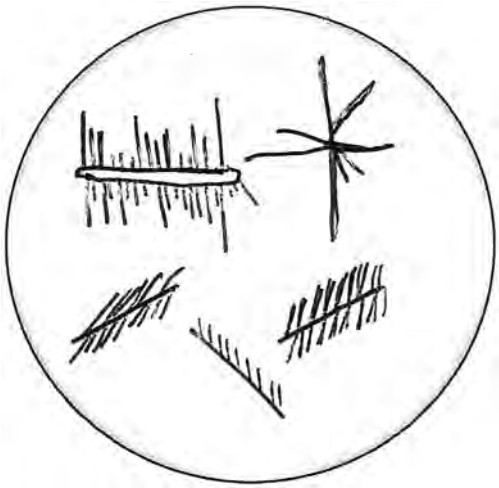
IR Spectrum

See Figure 6. Download SPC file.

PLM Optical Properties

Approximate Size Range	Main spines ≤ 5 µm width; > 100 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	$n_1 \approx 1.660$ and $n_2 > 1.700$ 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 filter paper.
Estimated Birefringence	High
Extinction*	Oblique (1°–41°); some parallel (0°)
Sign of Elongation*	Positive (+) and negative (−)
Interference Figure	Indeterminable

*Because extinction angles can be nearly 45°, the sign of elongation is often ambiguous (e.g. if the extinction angle is 45°, then the sign is neither + nor −). When the extinction angle closely approaches 41°, the usual alignment method for determining the sign of elongation (lower left to upper right) will not immediately yield an answer that is correct. Instead, rotate the stage until the crystal is in the extinction position, then rotate the stage 45° to the brightness position nearest to the usual alignment. If the Red I compensator is inserted and addition of retardation results, then the sign of elongation is positive (+).

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Cocaine: Gold Chloride with Hydrochloric Acid (continued)

Figure 2. 3 PPP of cocaine in 5 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent; crossed polars and Red I compensator. Note bright yellow interference colors when crystals are parallel to polars. Also, barbs on main rod are at oblique angles.

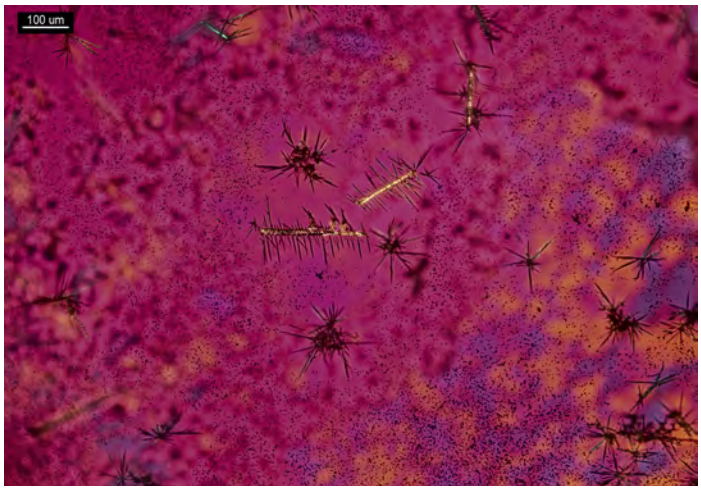

Figure 3. 1 PPP of cocaine in 5 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent; crossed polars and Red I compensator. Note bright yellow interference colors on center comb, indicating oblique extinction.

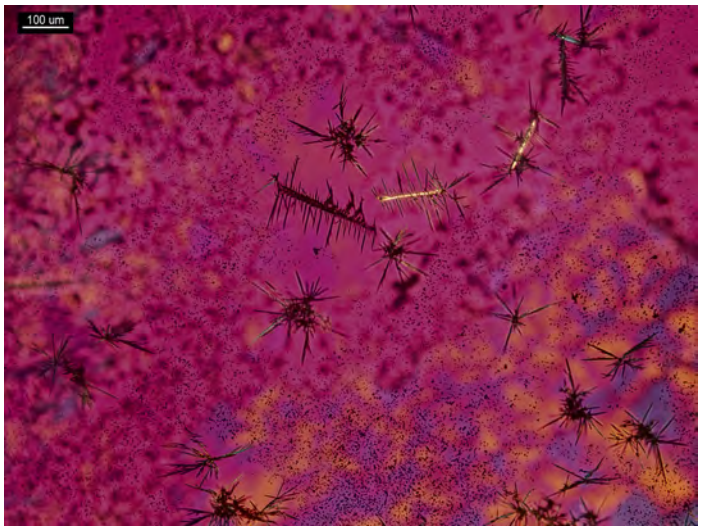

Figure 4. 1 PPP of cocaine in 5 µL of 10% HCl and 5 µL of $HAuCl_4$ reagent; crossed polars and Red I compensator. Note the center comb is at extinction position at an oblique angle.

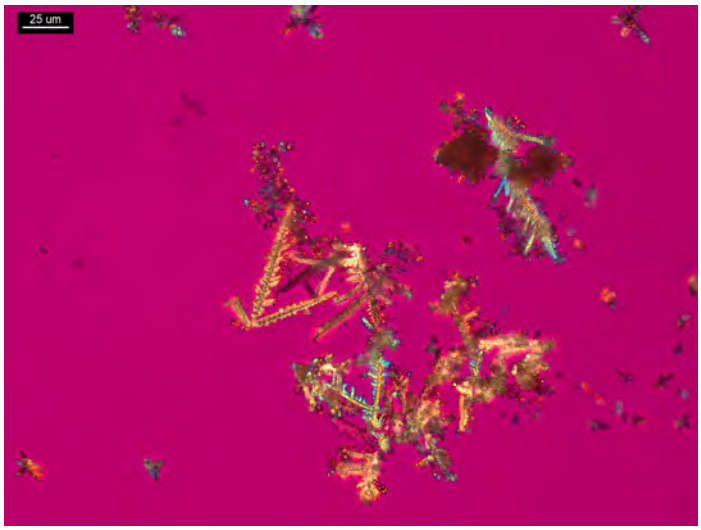

Figure 5. Hydroxyzine:cocaine, 1:5 in 5 µL of 10% HCl and 5 µL $HAuCl_4$. Cocaine with hydroxyzine is also detectable at 1:1 and 5:1, however, typical crystals can become distorted and unrecognizable after several minutes; crossed polars and Red I compensator.

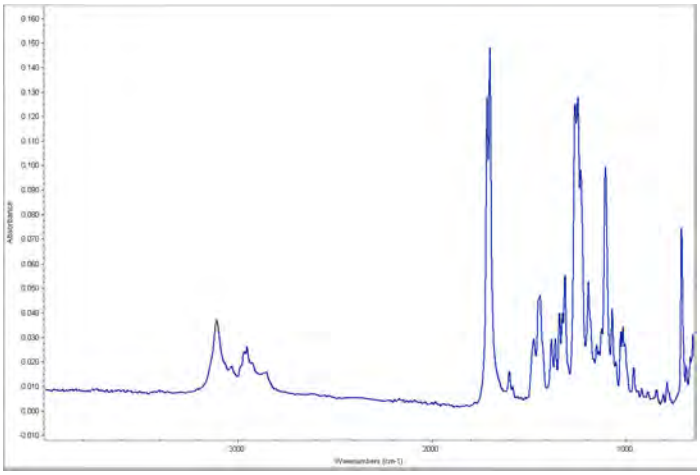

Figure 6. Infrared spectrum of cocaine gold chloride in hydrochloric acid precipitate. Download SPC file.

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Cocaine: Platinum Chloride with Acetic Acid

REAGENT 2A: Platinum Chloride (H_2PtCl_6) with Acetic Acid (HOAc)

5% aqueous: 1 g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 20 mL

Test Method

Direct test: Dissolve sample in 5 µL of 10% HOAc, then add 5 µL of reagent to the edge of the sample drop; no coverslip.

Reference

1. ASTM E1968-11: Standard Guide for Microcrystal testing in Forensic Analysis of Cocaine, ASTM International, 2011.

Limit of Detection

1 PPP

Time Required for Crystal Formation

2–5 minutes. Crystals will begin to deteriorate after ≈ 5 minutes.

Crystal Morphology and Test Notes

Feathery, spiny, combs, sometimes K- or V-shaped.

Photomicrograph of Typical Crystals

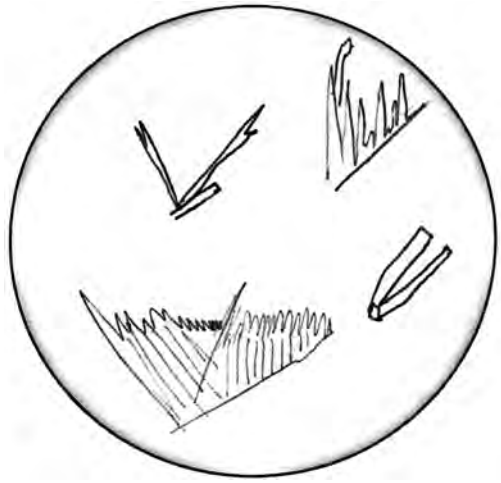
Figure 1. 1 PPP of cocaine in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Forms spiny, V-shaped crystals.

Pharmaceuticals, Adulterants or Other Drug Interactions

Common adulterants with cocaine that my inhibit or distort crystal formation include caffeine, levamisol and strychnine. The H_2PtCl_6 reagent is more sensitive than the $HAuCl_4$ reagent for the detection of cocaine in the presence of some adulterants. The detectability of cocaine with selected adulterants is listed below:

- Caffeine:cocaine – detectable at 1:5 and 1:1; undetectable at 5:1
- Hydroxyzine:cocaine – detectable at 1:5, 1:1 and 5:1
- Levamisol:cocaine – detectable at 1:5, 1:1; undetectable at 5:1
- Lidocaine:cocaine – detectable at 1:5, 1:1 and 5:1
- Phenacetin:cocaine – detectable at 1:5, 1:1 and 5:1
- Procaine:cocaine – detectable at 1:5, 1:1 and 5:1
- Strychnine:cocaine – undetectable at 1:5, 1:1 and 5:1

PLM Optical Properties

Approximate Size Range	Spine ≤ 5 µm width; > 50 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	$n_1 \approx 1.680$ and $n_2 \approx 1.570$–1.580 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 filter paper.
Estimated Birefringence	Moderate–High
Extinction	Parallel (0°) and oblique (1°–42°)
Sign of Elongation	Positive (+) and negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 13. Download SPC file.

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Cocaine: Platinum Chloride with Acetic Acid (continued)

Figure 2. Same as Figure 1; crossed polars.

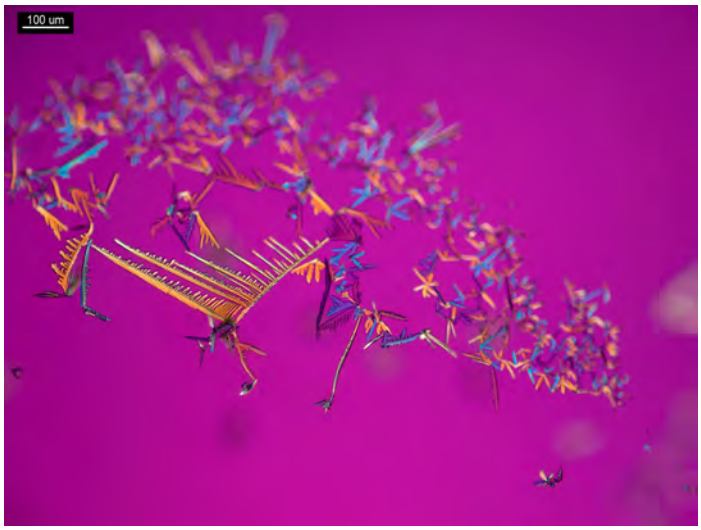

Figure 3. Same as Figure 1; crossed polars and Red I compensator.

Figure 4. Caffeine and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars and Red I compensator.

Figure 5. Hydroxyzine and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars and Red I compensator.

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Cocaine: Platinum Chloride with Acetic Acid (continued)

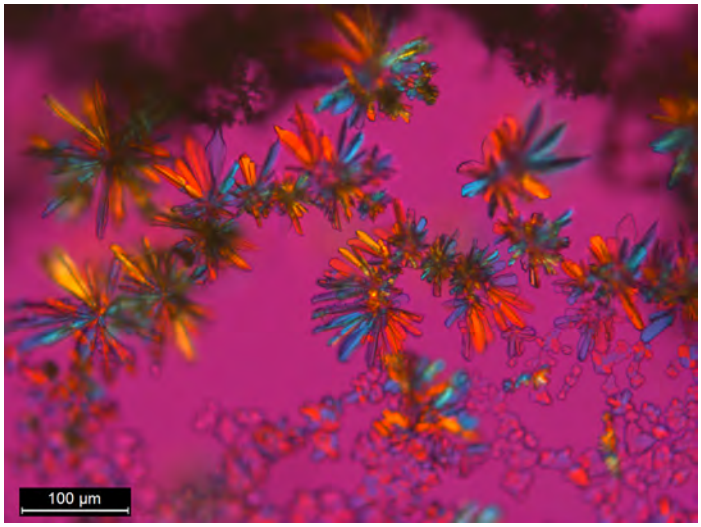

Figure 6. Levamisol (no cocaine) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form rosettes of blades; crossed polars and Red I compensator.

Figure 7. Levamisol and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Forms K-shaped crystals; crossed polars and Red I compensator.

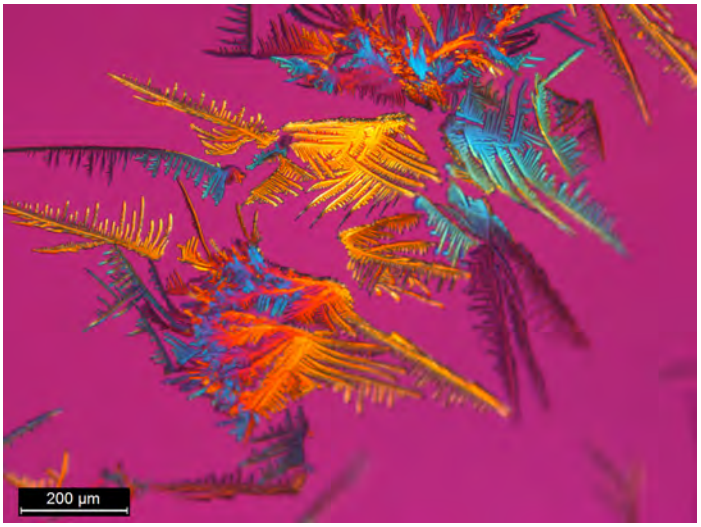

Figure 8. Lidocaine and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars and Red I compensator.

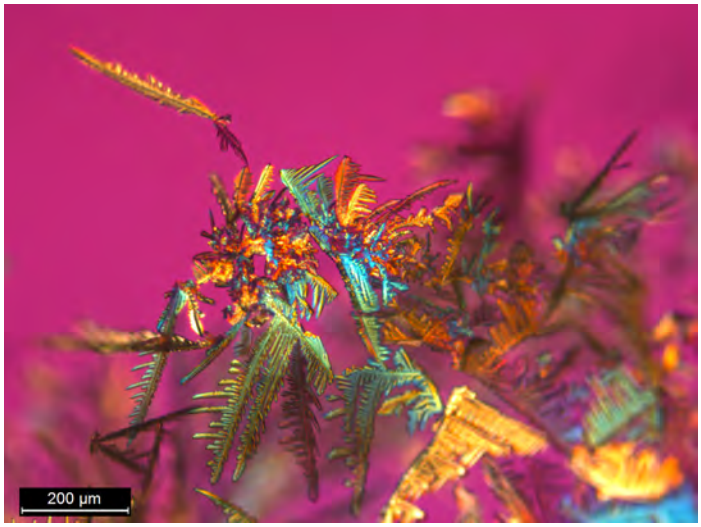

Figure 9. Lidocaine and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars and Red I compensator.

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Cocaine: Platinum Chloride with Acetic Acid (continued)

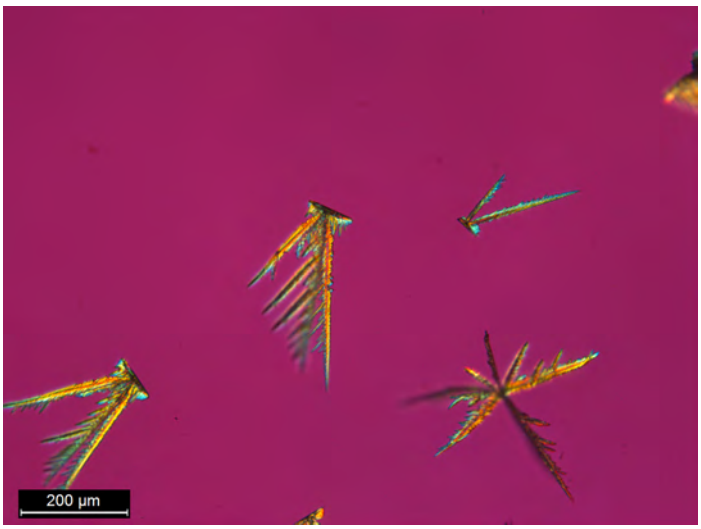

Figure 10. Phenacetin and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. V- and K-shaped crystals form; crossed polars and Red I compensator.

Figure 11. Procaine and cocaine (1:1) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars and Red I compensator.

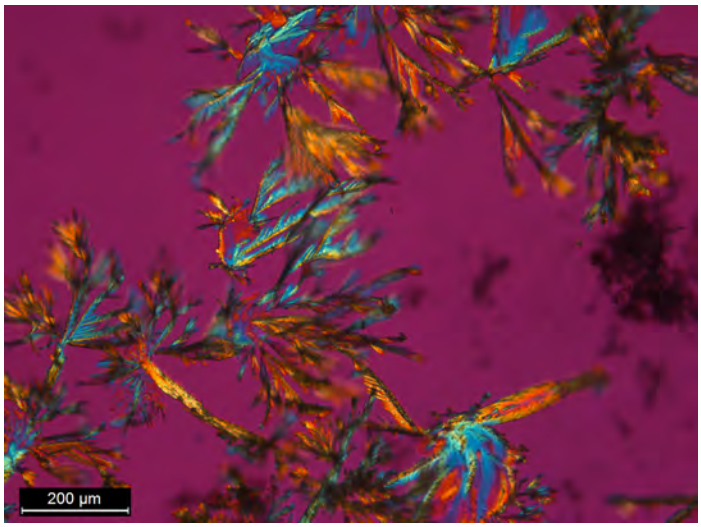

Figure 12. Strychnine and cocaine (1:5) in 5 µL 10% HOAc and 5 µL of H_2PtCl_6 reagent. Typical crystals of cocaine-platinum chloride with acetic acid are undetectable; crossed polars and Red I compensator.

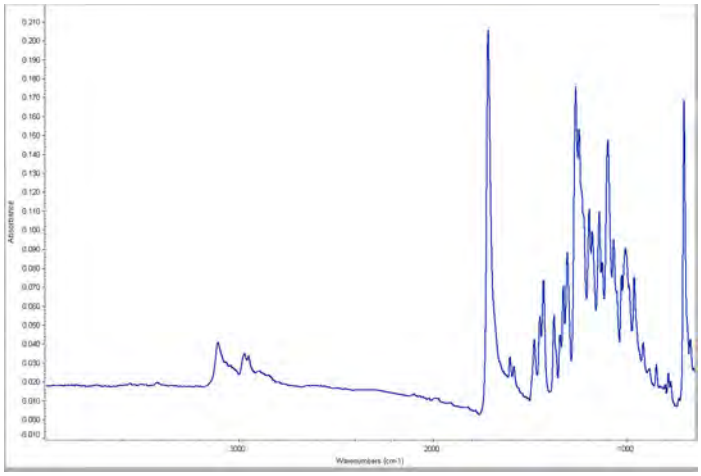

Figure 13. Infrared spectrum of cocaine platinum chloride with acetic acid precipitate. Download SPC file.

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Cocaine: Platinum Chloride with Hydrochloric Acid

REAGENT 2B: Platinum Chloride (H_2PtCl_6) with Hydrochloric Acid (HCl)

5% aqueous: 1 g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 20 mL

Test Method

Direct test: Dissolve sample in 5 µL of 10% HCl, then add 5 µL of reagent to the edge of the sample drop; no coverslip.

Reference

1. ASTM E1968-11: Standard Guide for Microcrystal testing in Forensic Analysis of Cocaine, ASTM International, 2011.

Limit of Detection

1 PPP

Time Required for Crystal Formation

2–5 minutes. Crystals will begin to deteriorate after ≈ 5 minutes.

Crystal Morphology and Test Notes

Dendritic, feathery, combs, sometimes K- and V-shaped.

Photomicrograph of Typical Crystals

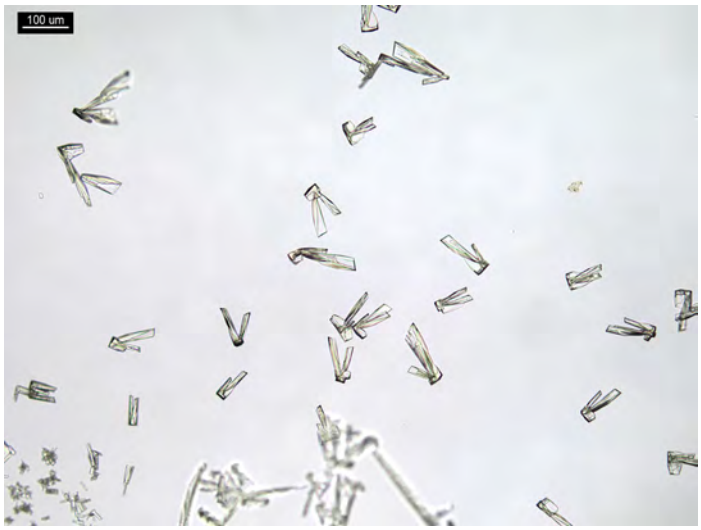


Figure 1. 1 PPP of cocaine in 5 µL 10% HCl and 5 µL of H_2PtCl_6 reagent. Crystals form K or V shapes.

Pharmaceuticals, Adulterants or Other Drug Interactions

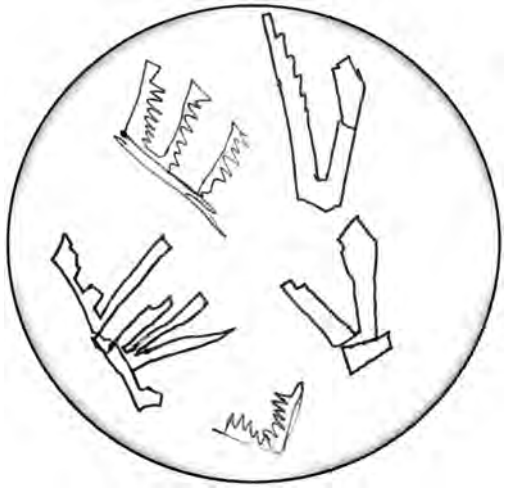
Common adulterants that may inhibit or distort crystal formation include caffeine, levamisol and strychnine. The H_2PtCl_6 reagent is more sensitive than the $HAuCl_4$ reagent for the detection of cocaine in the presence of some adulterants. The detectability of cocaine with selected adulterants is listed below:

- Caffeine:cocaine – detectable at 1:5 and 1:1; undetectable at 5:1
- Hydroxyzine:cocaine – detectable at 1:5, 1:1 and 5:1
- Levamisol:cocaine – detectable at 1:5, 1:1; undetectable at 5:1
- Lidocaine:cocaine – detectable at 1:5, 1:1 and 5:1
- Phenacetin:cocaine – detectable at 1:5, 1:1 and 5:1
- Procaine:cocaine – detectable at 1:5, 1:1 and 5:1
- Strychnine:cocaine – undetectable at 1:5, 1:1 and 5:1

PLM Optical Properties

Approximate Size Range	Spine ≤ 10 µm width; > 50 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	$n_1 \approx 1.680$ and $n_2 \approx 1.570–1.580$ 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 filter paper.
Estimated Birefringence	Moderate–High
Extinction	Parallel (0°) and oblique (1°–39°)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 5. Download SPC file.

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Cocaine: Platinum Chloride with Hydrochloric Acid (continued)

Figure 2. 1 PPP of cocaine in 5 µL 10% HCl and 5 µL of H_2PtCl_6 reagent. Crystals form feathery combs; crossed polars.

Figure 3. Same as Figure 2; crossed polars and Red I compensator.

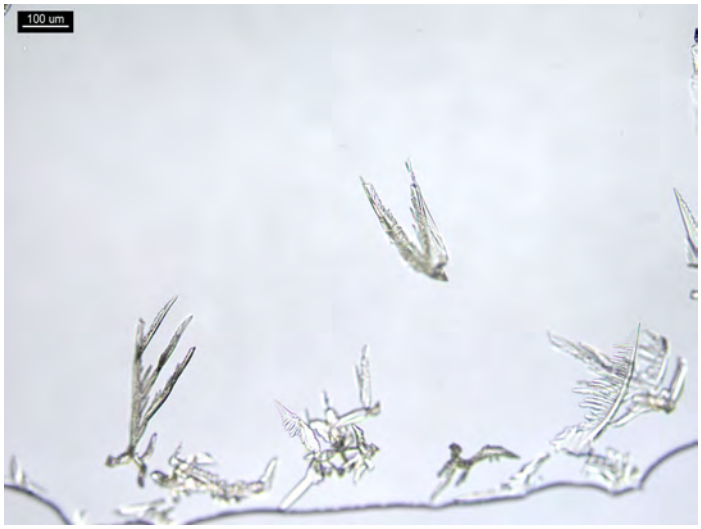

Figure 4. 1 PPP of cocaine in 5 µL 10% HCl and 5 µL of H_2PtCl_6 reagent. Forms feathery- and V-shaped crystals.

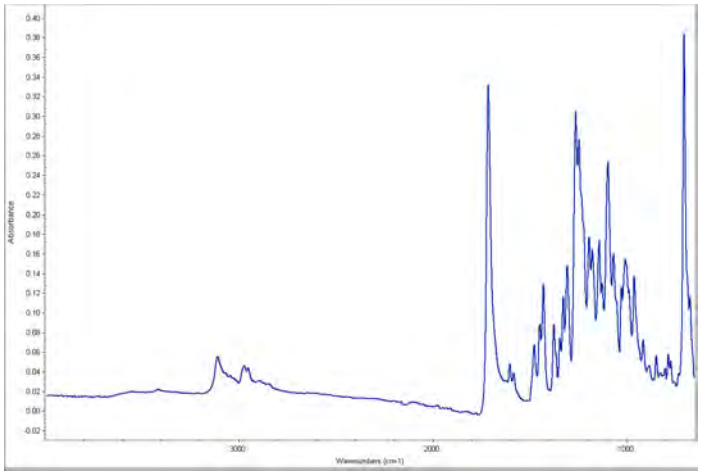

Figure 5. Infrared spectrum of cocaine platinum chloride with HCl precipitate. Download SPC file.

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Codeine: Marme's Reagent

REAGENT 1: Marme's Reagent – Cadmium Iodide (CdI_2) and Potassium Iodide (KI)

0.5 g CdI_2 and 1 g KI in 3 mL H_2O. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Add 5 µL of 1% HCl to sample on a glass slide. Place a 5 µL drop of reagent on a coverslip. Invert the coverslip and place it directly onto the sample. Or, add reagent directly to the sample drop; no coverslip.

References

1. Stephenson, C.H. *Microchemical Tests for Alkaloids*, Charles Griffin & Co., Ltd.: London, 1921.

Limit of Detection

1 PPP (5–10 PPP for some pharmaceutical tablets)

Time Required for Crystal Formation

Immediate (pharmaceutical tablets and oral solutions < 2 min.)

Crystal Morphology and Test Notes

Nearly equant tablets and prisms, and elongated prisms, often forming as rosettes. When no coverslip is used, prisms and rosettes are more elongated with fewer tablets. The typical equant tablets and prisms form over time.

Photomicrograph of Typical Crystals

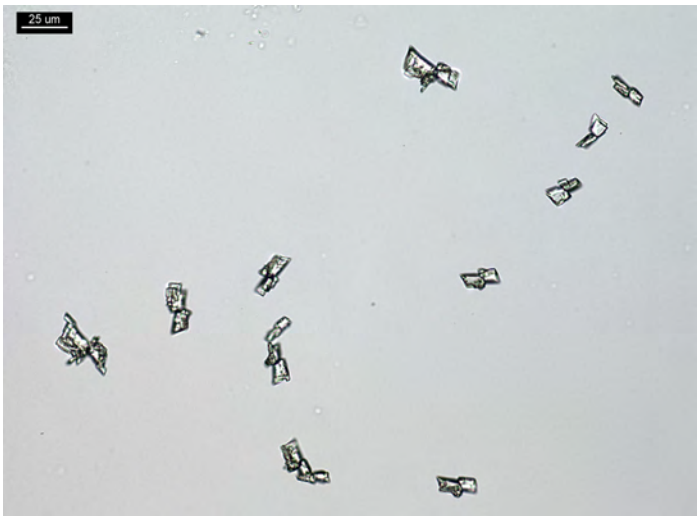


Figure 1. 1 PPP of codeine in 5 µL of 1% HCl and 5 µL of reagent, with coverslip. Crystals are equant tablets and prisms.

Pharmaceuticals, Adulterants or Other Drug Interactions

Tests were successful on the following pharmaceutical tablets that contain acetaminophen, buclizine or promethazine (5–10 PPP of the sample is required):

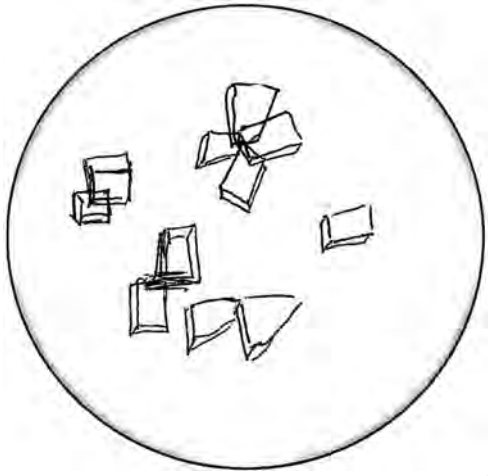
- 500 mg acetaminophen and 8 mg codeine
- 500 mg acetaminophen and 12.8 mg codeine
- 300 mg acetaminophen and 30 mg codeine
- 6.25 mg buclizine, 500 mg acetaminophen and 8 mg codeine

Tests were also successful on pharmaceutical oral solutions but required an acid-base extraction.

Acid-base extraction procedure: Add 100 µL of the oral solution to a microcentrifuge tube. Add 200 µL of 10% H_2SO_4 and mix by aspirating with a transfer pipette. Slowly add 200 µL of saturated Na_2CO_3 solution and mix. 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. Allow to evaporate, then proceed with microcrystal test. An acid-base extraction also works on small portions of pharmaceutical tablets.

- Codeine phosphate oral solution: 120 mg acetaminophen, 7% ethanol and 12 mg codeine
- Codinex™ oral solution: 15 mg/5 mL codeine phosphate, equivalent to 11.8 mg codeine
- Phenergan® oral solution: 6.25 mg promethazine and 10 mg codeine

PLM Optical Properties

Approximate Size Range	5–20 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	Indeterminable; dried crystals were obscured by recrystallization of the reagent. Crystals have high contrast in the test drop.
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Dried crystals were obscured by recrystallization of reagent.
Estimated Birefringence	Moderate
Extinction	Oblique (28°); some undulose
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Codeine: Marme's Reagent (continued)

Figure 2. 1 PPP of codeine in 5 µL of 1% HCl and 5 µL of reagent, with coverslip. Crystals form high-contrast, nearly equant tablets, prisms and rosettes; crossed polars and Red I compensator.

Figure 3. 5 PPP from a 300 mg acetaminophen and 30 mg codeine tablet in 5 µL of 1% HCl and 5 µL of reagent, with coverslip. Crystals form high-contrast, elongated prisms and rosettes are visible; crossed polars and Red I compensator.

Figure 4. Phenergan oral solution (6.25 mg promethazine and 10 mg codeine) after an acid-base extraction in 5 µL of 1% HCl and 5 µL of reagent, with coverslip. Crystals form high-contrast, nearly equant tablets, prisms and rosettes.

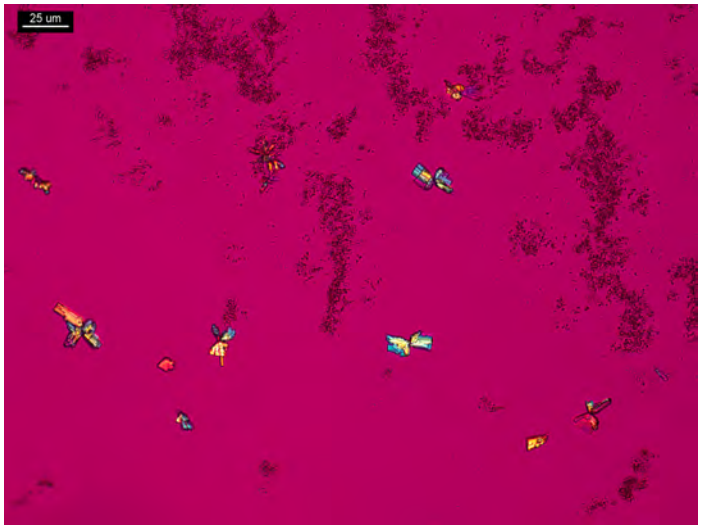

Figure 5. Same as Figure 4; crossed polars and Red I compensator.

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Codeine: Marme's Reagent (continued)

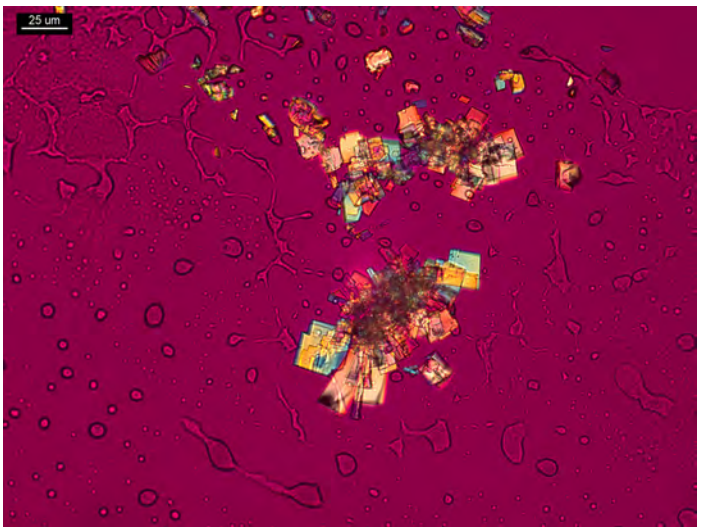

Figure 6. Codinex™ oral solution (codeine phosphate 15 mg/ 5 mL) after an acid-base extraction in 5 µL of 1% HCl and 5 µL of reagent. Crystals form tablets; crossed polars and Red I compensator.

Figure 7. Oral solution (12 mg codeine phosphate, 120 mg aceteminophen, 7 % ethanol) after an acid-base extraction in 5 µL of 1% HCl and 5 µL of reagent. Crystals form prisms; crossed polars and Red I compensator.

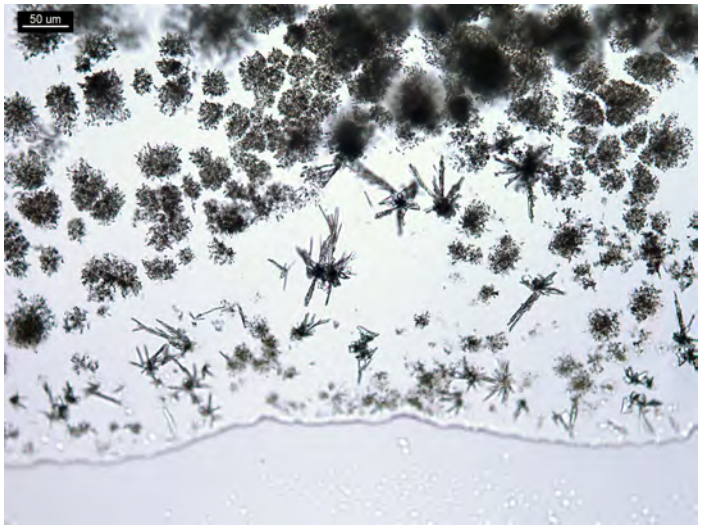

Figure 8. 1 PPP of codeine in 5 µL of 1% HCl and 5 µL of reagent, no coverslip. Crystals form high-contrast, more elongated prisms and rosettes with fewer tablets.

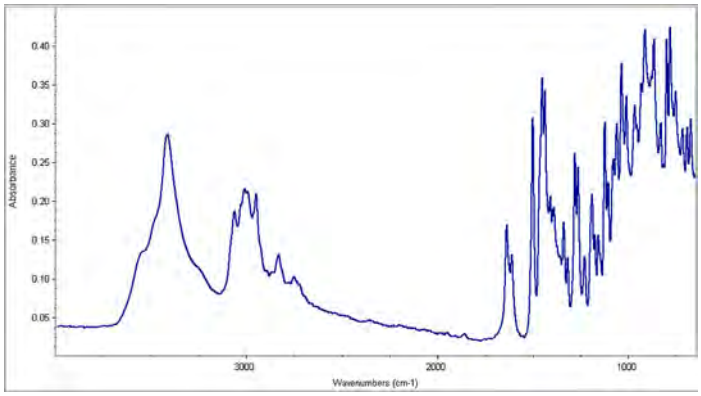

Figure 9. Infrared spectrum of codeine Marme's reagent precipitate. Download SPC file.

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Codeine: Fulton's O-2

REAGENT 2: Fulton's O-2 (I-KI)

0.4 mL I-KI solution (0.1 g I_2 and 0.35 g KI in 1 mL H_2O). 1.6 mL H_2O, 2.0 mL glacial HOAc and 2.0 mL concentrated H_3PO_4. This reagent has a shelf life of several weeks to several months. It should be dark brown and free of precipitates.

Test Method

Direct test: Place the sample on a slide and crush it with a pipette tip, glass rod or toothpick. Place a 10 µL drop of reagent on a coverslip; invert the coverslip and place it directly onto the sample.

References

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

Limit of Detection

1 PPP (1–10 PPP for some pharmaceutical tablets)

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Hatchet blades, hourglasses, triangles, semi-circles, trapezoids and rosettes of these same shapes. Amorphous grains precede crystal formation.

Photomicrograph of Typical Crystals

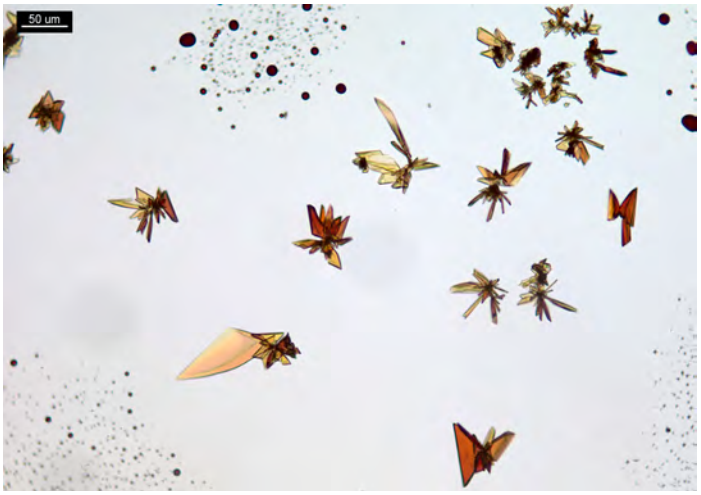


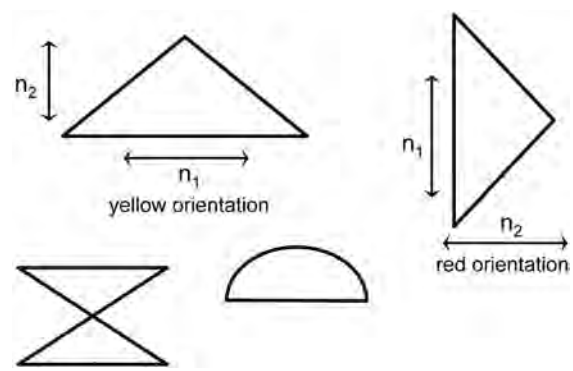
Figure 1. 1 PPP of codeine and 10 µL of reagent. Crystals form rosettes of triangles and hatchet blades.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on some pharmaceutical tablets. An acid-base extraction may be helpful. Results were not always successful or reproducible, especially when an abundance of starch is present. Immiscible, oily drops preceded crystal formation, however, with some pharmaceuticals, typical crystals never formed. The test was unsuccessful with pharmaceutical oral solutions.

Acid-base extraction procedure: Add a portion of the pharmaceutical tablet to a microcentrifuge tube. Add 200 µL of 10% H_2SO_4 and mix by aspirating with a transfer pipette. Slowly add 200 µL of saturated Na_2CO_3 solution and mix. 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. Allow to evaporate, then proceed with microcrystal test.

PLM Optical Properties

Approximate Size Range	5–30 µm; increases over time
Color/Pleochroism	Red-orange. Pleochroic; rusty red-orange to yellow
Refractive Indices (RI)	$n_1 \approx 1.650–1.674$ $n_2 > 1.700$
Morphology Illustration	
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with chloroform using a tungsten needle.
Estimated Birefringence	High
Extinction	Symmetrical or parallel to one edge of triangle
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 13. Download SPC file.

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Codeine: Fulton's O-2 (continued)

Figure 2. 1 PPP of codeine and 10 µL of reagent. Crystals form rosettes of triangles.

Figure 3. Same as Figure 2; crossed polars and Red I compensator.

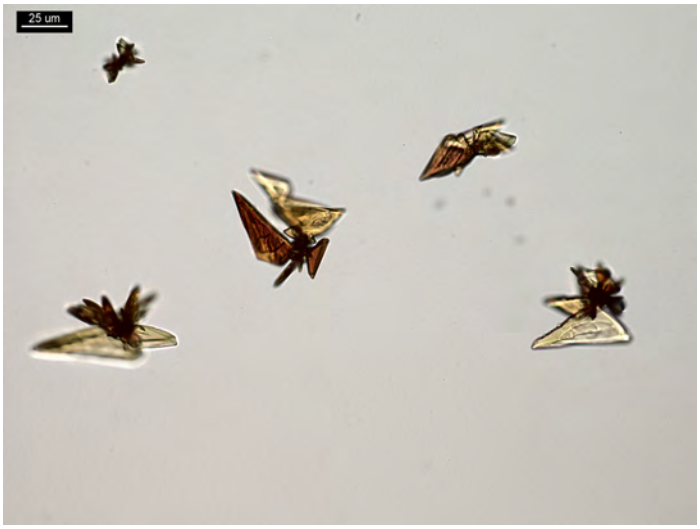

Figure 4. 1 PPP of codeine and 10 µL of reagent. Crystals form rusty red/orange to yellow pleochroic rosettes of triangles; microscope polarizer is oriented East-West.

Figure 5. Same as Figure 4. Microscope polarizer is oriented North-South.

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Codeine: Fulton's O-2 (continued)

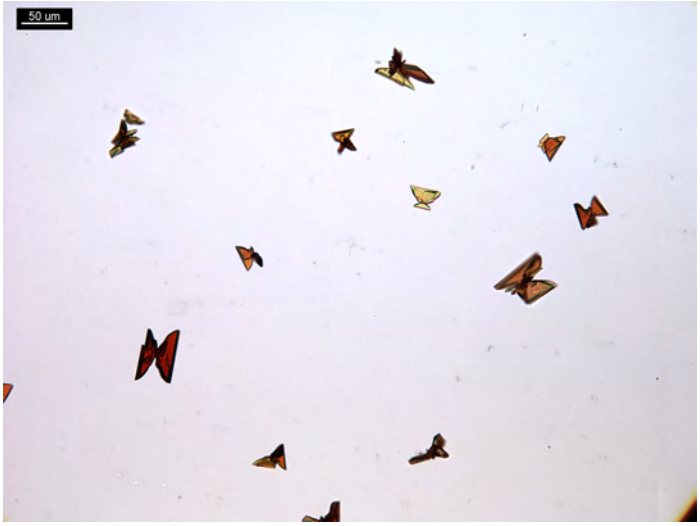

Figure 6. 1 PPP of codeine and 10 µL of reagent. Crystals form hourglass- and semicircle-shaped crystals.

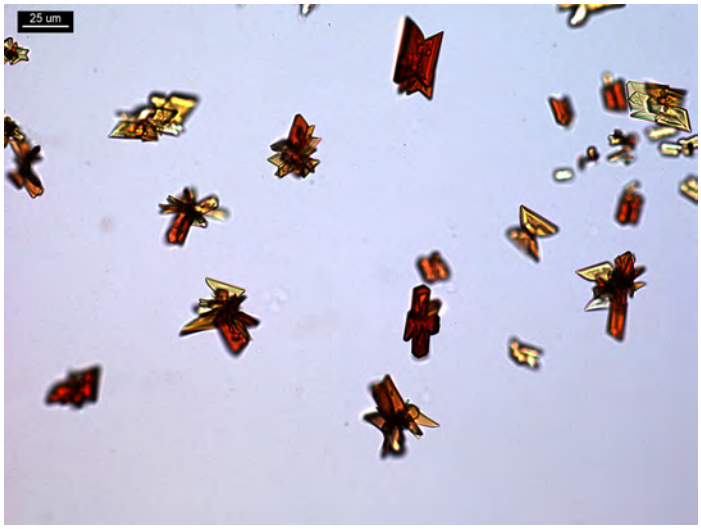

Figure 7. 1 PPP of codeine and 10 µL of reagent. Crystals form rosettes of trapezoids and semicircle-shaped crystals.

Figure 8. 5 PPP from a 30 mg codeine, 300 mg acetaminophen pharmaceutical tablet after an acid-base extraction and 10 µL of reagent. Crystals form rusty red/orange to yellow pleochroic rosettes.

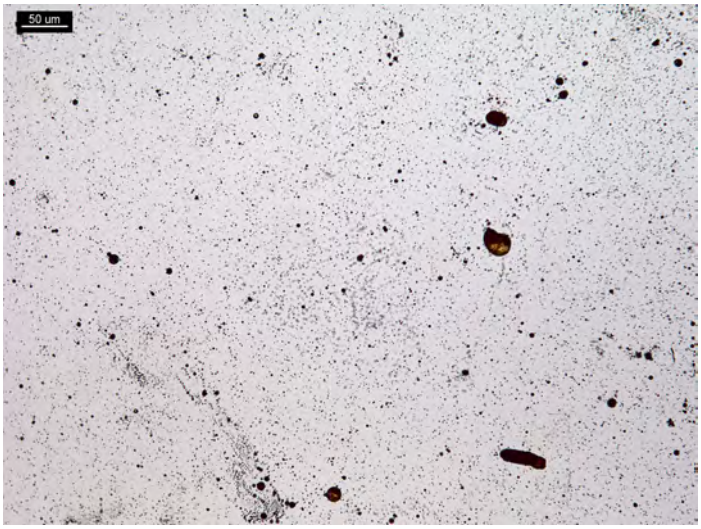

Figure 9. 100 µL of Codinex™ oral solution (15 mg/5 mL codeine phosphate) after an acid-base extraction and 10 µL of reagent. Immiscible oily drops are visible.

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Codeine: Fulton's O-2 (continued)

Figure 10. 5 PPP from a 30 mg codeine, 500 mg acetaminophen pharmaceutical tablet after an acid-base extraction and 10 µL of reagent. Initially, only immiscible oily drops developed. Additional crystallization resulted after applying back-and-forth pressure to the coverslip with a pencil eraser.

Figure 11. 5 PPP from a 30 mg codeine, 500 mg acetaminophen pharmaceutical tablet after an acid-base extraction and 10 µL of reagent. Immiscible oily drops developed immediately, but initially only one single crystal formed. Further crystallization was induced by pushing the coverslip back and forth while applying pressure with a pencil eraser.

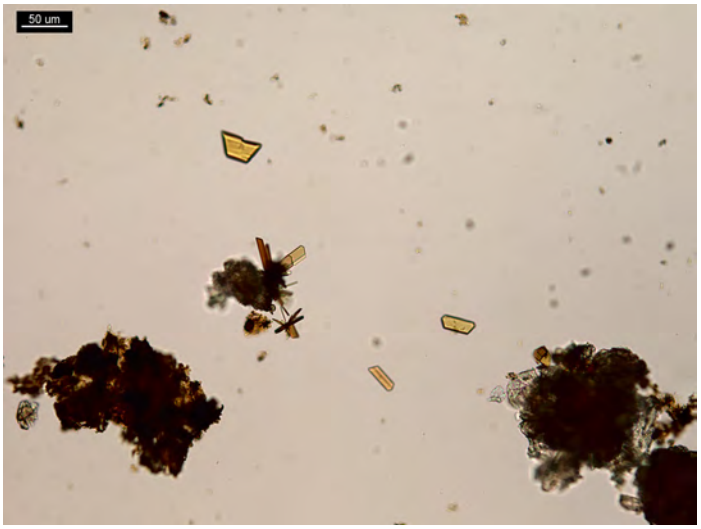

Figure 12. 5 PPP from a 8 mg codeine, 6.25 mg buclizine, 500 mg acetaminophen pharmaceutical tablet and 10 µL of reagent. Crystals form trapezoids and rosettes of trapezoids.

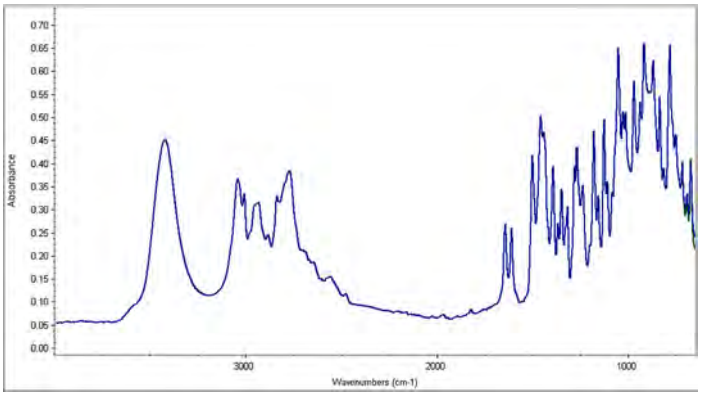

Figure 13. Infrared spectrum of codeine Fulton's O-2 reagent precipitate. Download SPC file.

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Codeine: Fulton's C-3

REAGENT 3: Fulton's C-3 (I-KI)

0.3 mL I-KI solution (0.1 g I_2 + 0.1 g KI in 1 mL H_2O), 2.4 mL H_2O, 1.5 mL glacial HOAc and 0.3 mL dilute H_2SO_4 (0.1 mL H_2SO_4 + 0.3 mL H_2O). Reagent does not keep and should be fresh when used.

Test Method

Direct test: Place the sample on a slide and add a 5 µL drop of reagent; crush and stir gently with a pipette tip, glass rod or toothpick. An acid-base extraction may be necessary for some pharmaceutical tablets and oral solutions. Reagent is light sensitive.

References

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

Limit of Detection

1 PPP (1–10 PPP for some pharmaceutical tablets)

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Triangles and rosettes of rods and triangles. Immiscible oily drops precede crystal formation. Crystal morphology is similar to codeine with Fulton's O-2 reagent.

Photomicrograph of Typical Crystals

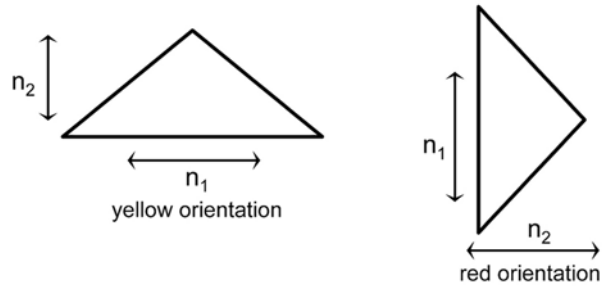
Figure 1. 1 PPP of codeine and 5 µL of reagent. Amorphous grains precede crystal formation. Crystals form triangles and rosettes of triangles.

Pharmaceuticals, Adulterants or Other Drug Interactions

An acid-base extraction was necessary for pharmaceutical tablets and oral solutions. However, results were not always successful or reproducible, especially in oral solutions or when an abundance of starch is present in a tablet. Oral solutions, after acid-base extraction, form rosettes of rods followed by triangles. Some pharmaceuticals formed distorted rosettes of flakes, rods or irregular plates.

Acid-base extraction procedure: Add 200 µL of the oral solution to a microcentrifuge tube. Add 200 µL of 10% H_2SO_4 and mix by aspirating with a transfer pipette. Slowly add 200 µL of saturated Na_2CO_3 solution and mix. 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. Allow to evaporate, then proceed with microcrystal test.

PLM Optical Properties

Approximate Size Range	10 µm; increases to more than 50 µm within one minute
Color/Pleochroism	Rusty red. Pleochroic; rusty red to yellow
Refractive Indices (RI)	n_1 = 1.650–1.670 n_2 > 1.700
Morphology Illustration	
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with lab tissue then washed with chloroform using a tungsten needle.
Estimated Birefringence	High
Extinction	Symmetrical or parallel to one edge of triangle
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 11. Download SPC file.

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Codeine: Fulton's C-3 (continued)

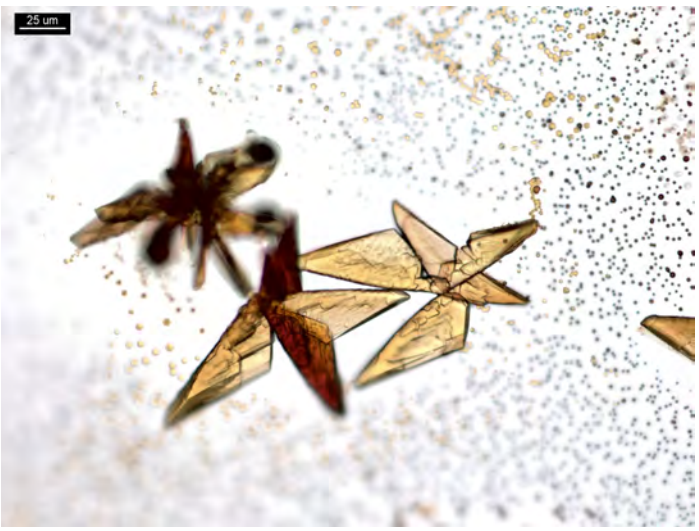

Figure 2. 1 PPP of codeine and 5 µL of reagent. Crystals form rusty red to yellow pleochroic rosettes of triangles; microscope polarizer is oriented East-West.

Figure 3. Same as Figure 2. Microscope polarizer is oriented North-South.

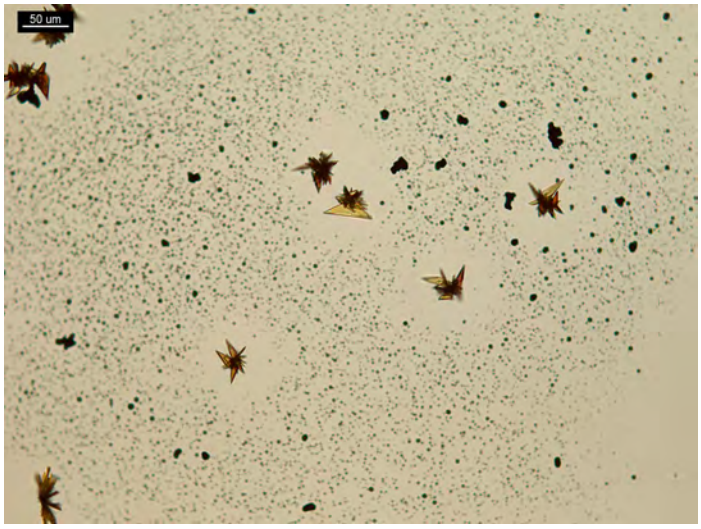

Figure 4. 1 PPP of codeine and 5 µL of reagent. Immiscible oily drops precede crystal formation. Crystals form rosettes of triangles, and some rosettes of rods are also visible (left and lower left).

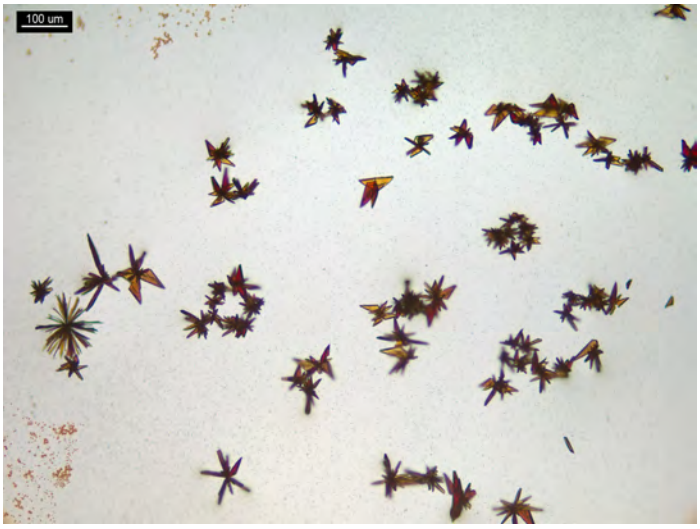

Figure 5. 1 PPP of codeine and 5 µL of reagent. Crystals form rosettes of triangles and rods.

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Codeine: Fulton's C-3 (continued)

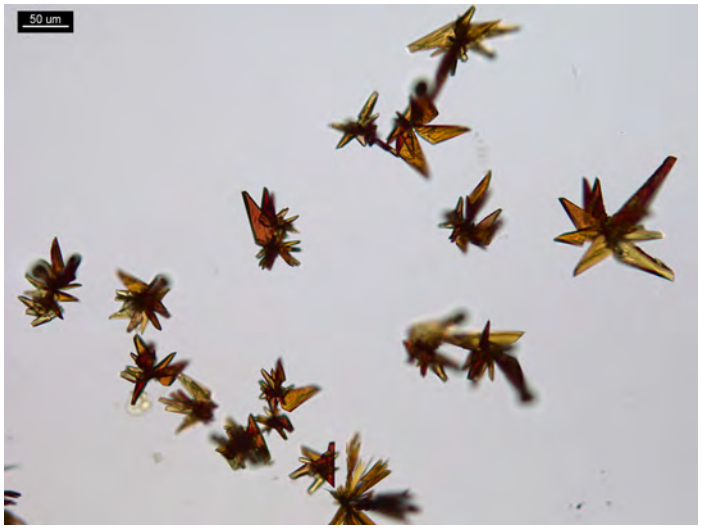

Figure 6. 1 PPP of codeine and 5 µL of reagent. Crystals form rosettes of triangles and rods.

Figure 7. 1 PPP of codeine and 5 µL of reagent. Crystals form rosettes of triangles and rods.

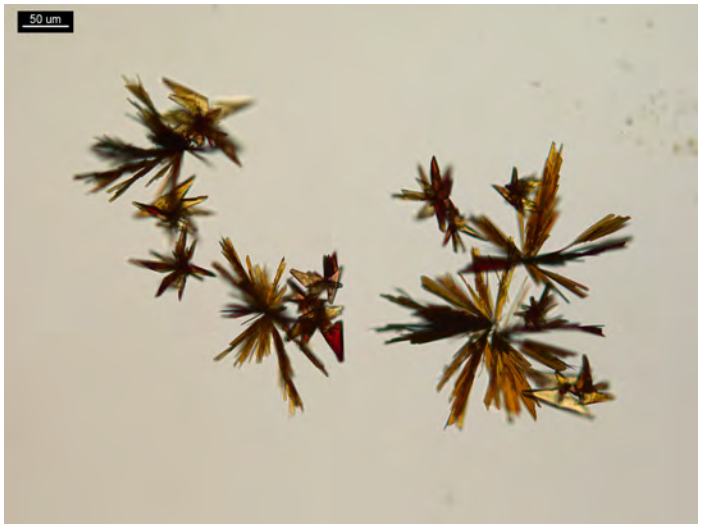

Figure 8. 1 PPP of codeine and 5 µL of reagent. Crystals form rosettes of triangles and rods.

Figure 9. 8 PPP from a 30 mg codeine, 300 mg acetamino-phen pharmaceutical tablet and 5 µL of reagent. Crystals form rosettes of angular plates and triangles. An acid-base extraction produced similar crystals.

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Codeine: Fulton's C-3 (continued)

Figure 10. 8 PPP from a 8 mg codeine, 500 mg acetaminophen pharmaceutical tablet and 5 µL of reagent. Crystals form rosettes of angular plates, elongated flakes and triangles.

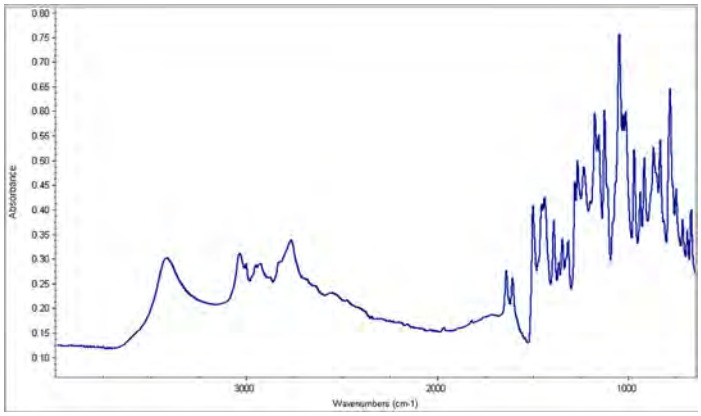

Figure 11. Infrared spectrum of codeine Fulton's C-3 reagent precipitate. Download SPC file.

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Diazepam: Platinum Chloride

REAGENT 1: Platinum Chloride (H_2PtCl_6)

5% aqueous: 1 g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 20 mL

Test Method

Direct test: Dissolve sample in 0.1 N HCl, then add 5 µL reagent; coverslip optional.

References

1. Haynes, W.S. "On the Development of Microcrystal Tests for Some 1,4-Benzodiazepines," M.S. Thesis, California State University, Los Angeles, 2000.

Limit of Detection

1 PPP

Time Required for Crystal Formation

3–6 minutes

Crystal Morphology and Test Notes

Sheaves and rosettes of needles are mostly observed at the perimeter of the drop. Needles are very thin and taper to a point.

Photomicrograph of Typical Crystals

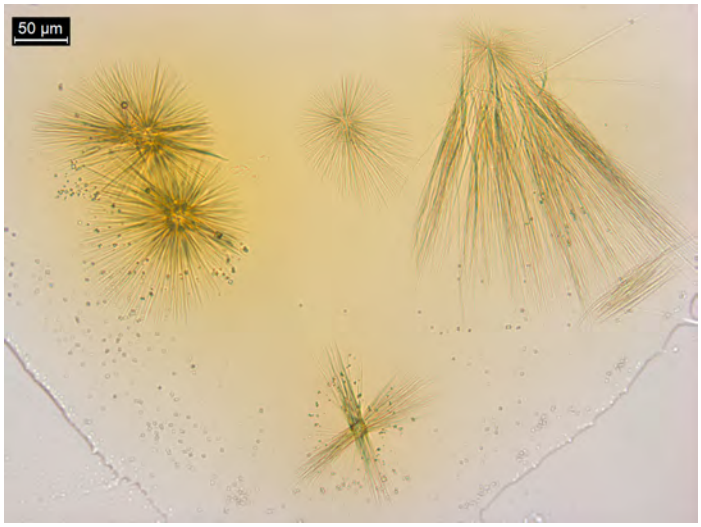


Figure 1. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form sheaves and rosettes of needles.

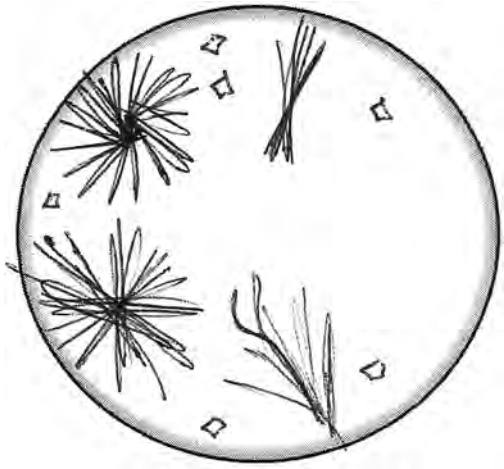
Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on a 2 mg tablet using 1 PPP of tablet material; typical crystals formed after ≈ 4 minutes. This test was also successful after a chloroform extraction on a Diastat® rectal gel containing 2.5 mg/0.5 mL of diazepam: Place a 0.5 cm diameter portion of gel in a spot plate, then add several drops of chloroform and stir with a pipette tip, glass rod or toothpick. With a micropipette, extract and transfer 5 µL to a glass slide. The direct test can be performed on the residue after the chloroform evaporates. Typical crystals formed after 5 minutes.

PLM Optical Properties

Approximate Size Range	1–2 µm width, 50 to > 100 µm length
Color/Pleochroism	Pale yellow; not pleochroic
Refractive Indices (RI)	n-parallel: 1.690–1.700 n-perpendicular: 1.690–1.700

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Crystals were gently heated then washed with water using a tungsten needle and dried at room temperature.
Estimated Birefringence	Low
Extinction	Oblique (40°)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 8. Download SPC file.

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Diazepam: Platinum Chloride (continued)

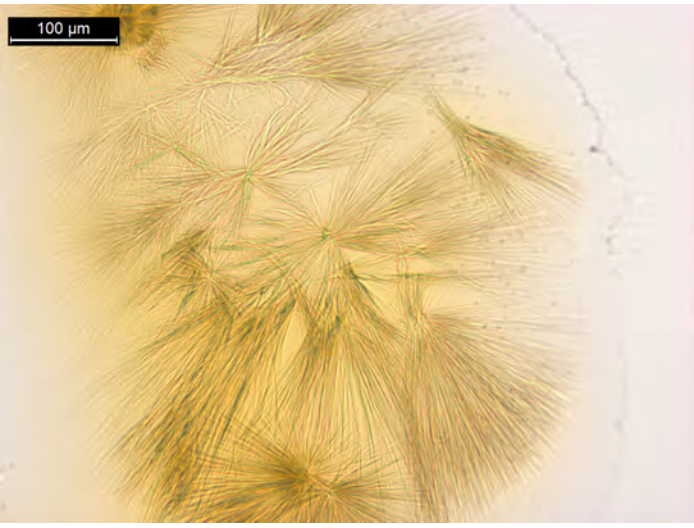

Figure 2. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form sheaves and rosettes of needles.

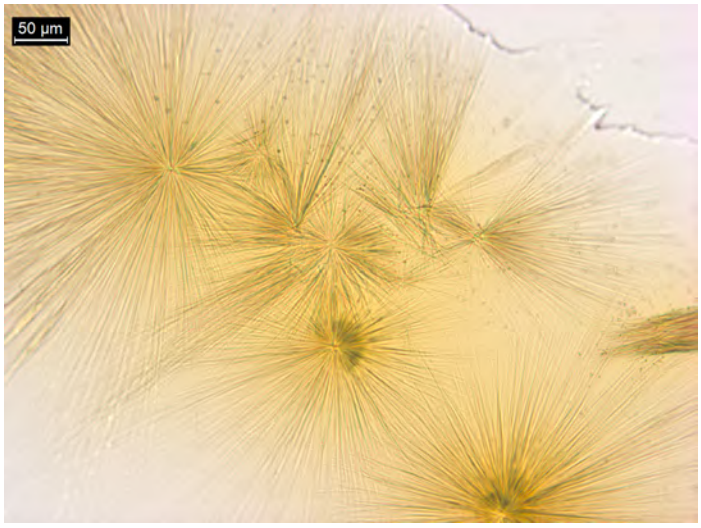

Figure 3. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form sheaves and rosettes of needles.

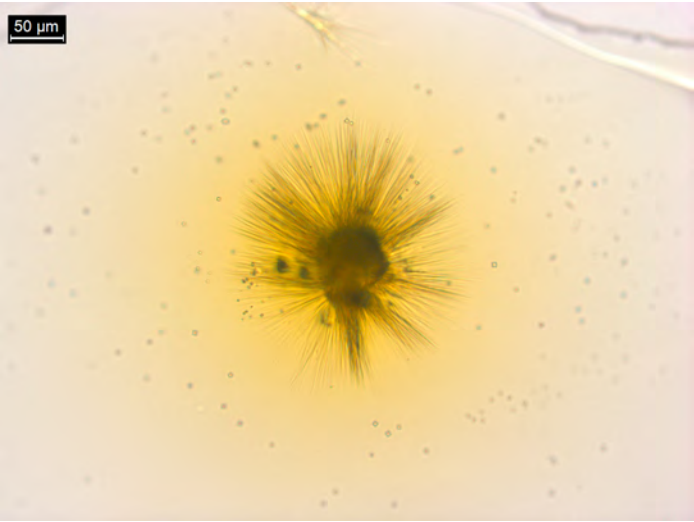

Figure 4. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form rosettes of needles.

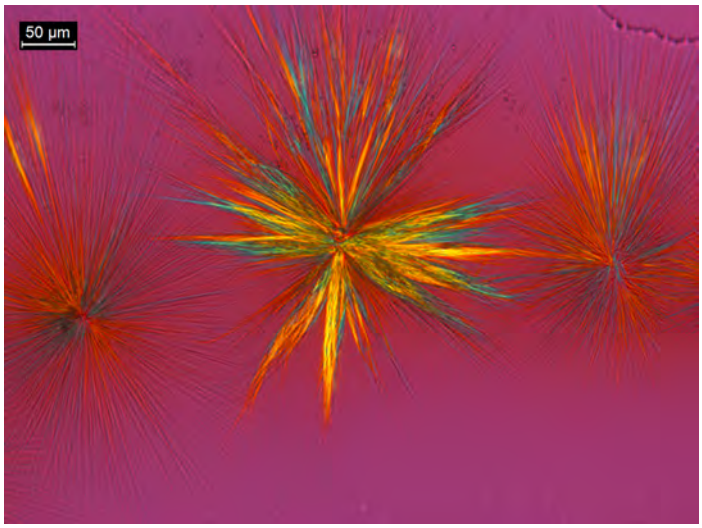

Figure 5. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form rosettes of needles; crossed polars and Red I compensator.

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Diazepam: Platinum Chloride (continued)

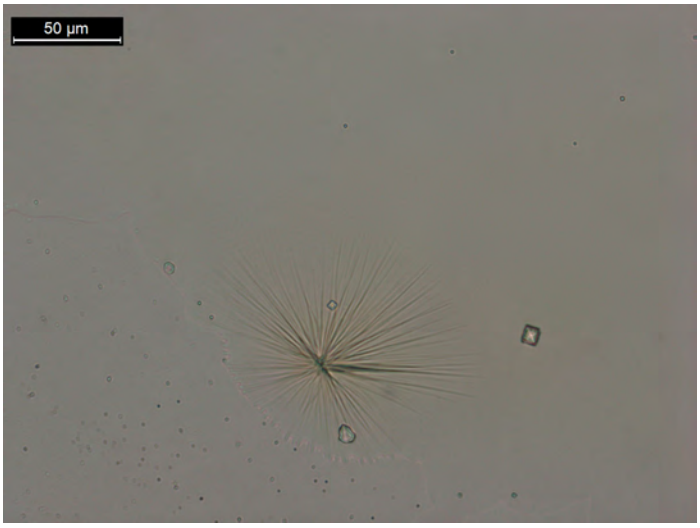

Figure 6. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form rosettes of needles.

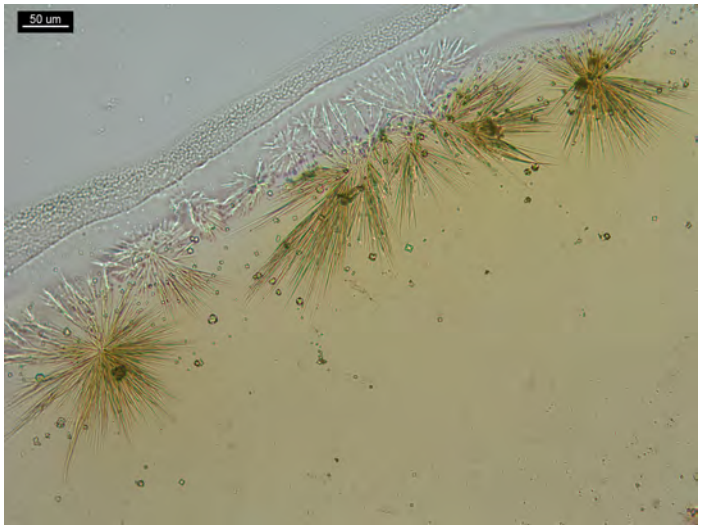

Figure 7. 1 PPP of diazepam dissolved in 0.1 N HCl and 5 µL of H_2PtCl_6 reagent. Crystals form rosettes of needles.

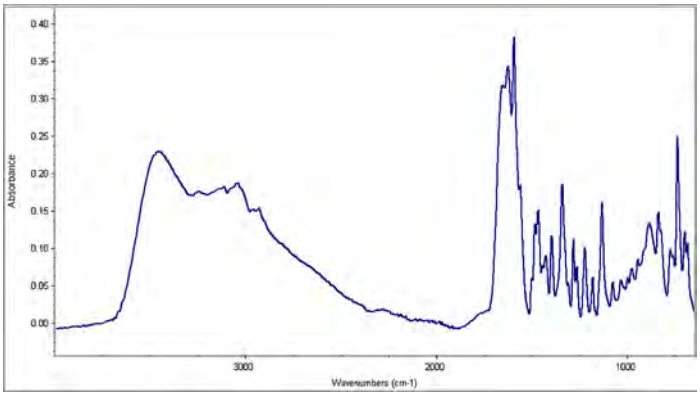

Figure 8. Infrared spectrum of diazepam platinum chloride precipitate. Download SPC file.

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Diazepam: Ammonium Thiocyanate

REAGENT 2: Ammonium Thiocyanate (NH_4SCN)

10% aqueous: 1 g NH_4SCN in H_2O, make up to 10 mL

Test Method

Direct test: Dissolve sample in 5 µL of 1% HCl on a glass slide. Place a 5 µL drop of reagent on a coverslip, invert and drop directly onto the sample.

References

1. Haynes, W.S. "On the Development of Microcrystal Tests for Some 1,4-Benzodiazepines," M.S. Thesis, California State University, Los Angeles, 2000.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Rosettes of thin blades and branched blades. Note: Typical crystals may form around undissolved diazepam.

Photomicrograph of Typical Crystals

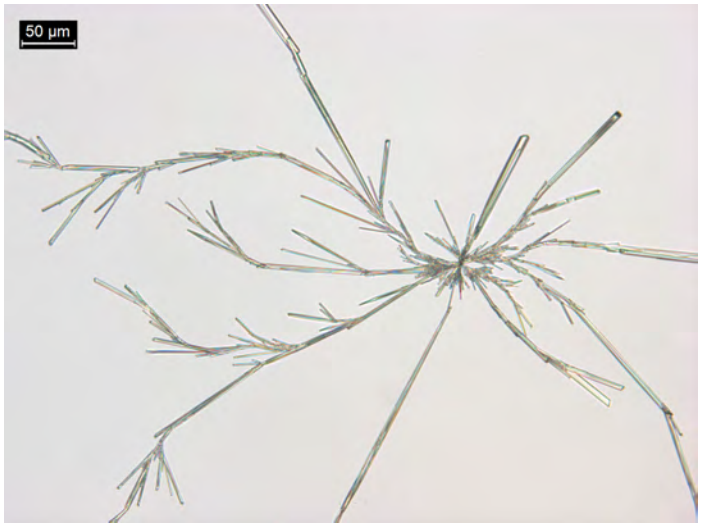
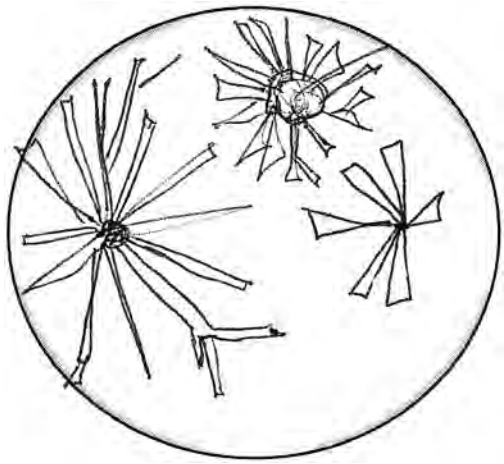


Figure 1. 1 PPP of diazepam dissolved in 5 µL of 1% HCl and 5 µL of NH_4SCN reagent. Crystals form rosettes of thin and branched blades.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on a 2 mg diazepam pharmaceutical tablet using 5 PPP of tablet material. This test was also successful after a chloroform extraction on a Diastat® rectal gel containing 2.5 mg/0.5 mL of diazepam: Place a 0.5 cm diameter portion of gel in a spot plate, then add several drops of chloroform and stir with a pipette tip, glass rod or toothpick. With a micropipette, extract and transfer 5 µL to a glass slide. The direct test can be performed on the residue after the chloroform evaporates. Typical crystals formed after 5 minutes. However, the results with this reagent on the rectal gel were not always reproducible, and in some cases, even after an hour, there were no recognizable crystals.

PLM Optical Properties

Approximate Size Range	2.5–10 µm width; 50 to >100 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel: 1.584 n-perpendicular: 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature then washed with chloroform using a tungsten needle.
Estimated Birefringence	High
Extinction	Parallel; oblique (7°)
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 7. Download SPC file.

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Diazepam: Ammonium Thiocyanate (continued)

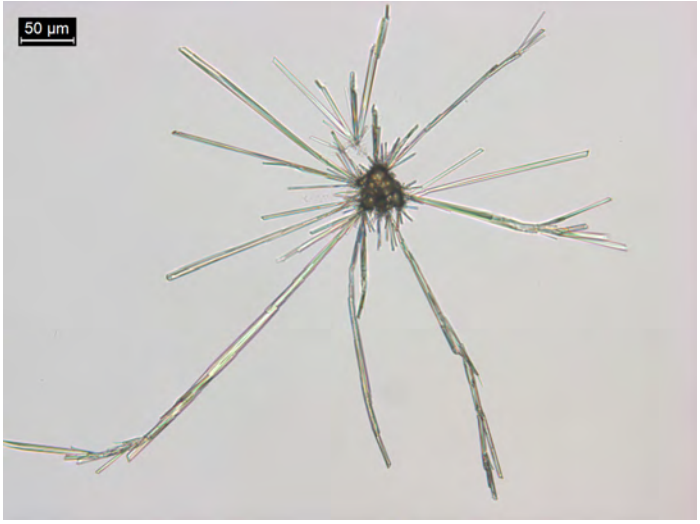

Figure 2. 1 PPP of diazepam dissolved in 5 µL of 1% HCl and 5 µL of NH_4SCN reagent. Crystals form rosettes of blades.

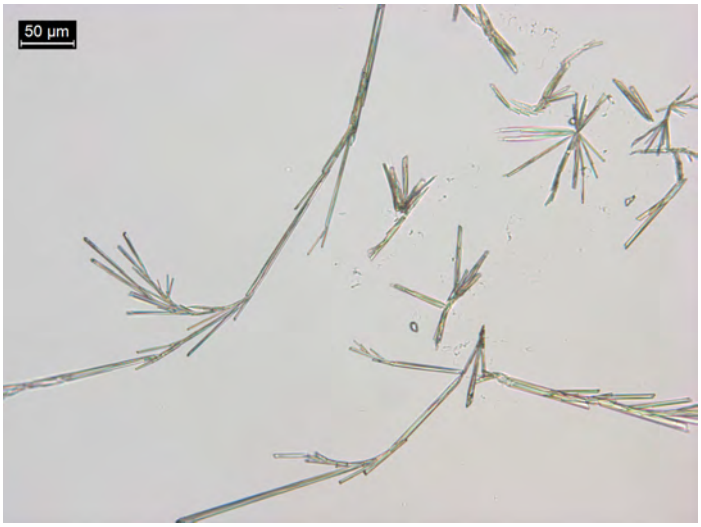

Figure 3. 1 PPP of diazepam dissolved in 5 µL of 1% HCl and 5 µL of NH_4SCN reagent. Crystals form rosettes of thin and branched blades.

Figure 4. 1 PPP of diazepam dissolved in 5 µL of 1% HCl and 5 µL of NH_4SCN reagent. Crystals form rosettes of blades.

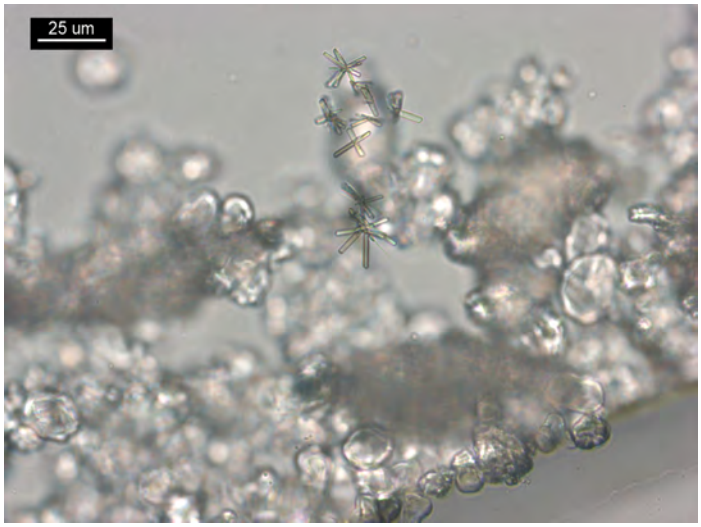

Figure 5. 5 PPP of tablet material from a 2 mg diazepam pharmaceutical tablet dissolved in 5 µL of 1% HCl and 5 µL of NH_4SCN reagent. Crystals form rosettes of blades.

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Diazepam: Ammonium Thiocyanate (continued)

Figure 6. Rectal gel containing 2.5 mg/0.5 mL of diazepam and 5 µL of 1% HCl and 5 µL of NH_4SCN reagent, after chloroform extraction. Crystals form branched blades.

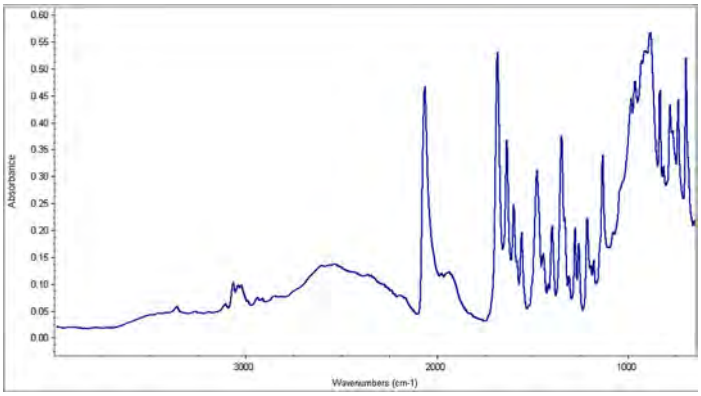

Figure 7. Infrared spectrum of diazepam ammonium thiocyanate precipitate. Download SPC file.

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l-Ephedrine: Gold Bromide

REAGENT 1: Gold Bromide ($HAuBr_4$)

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 60 mL of concentrated phosphoric acid. 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 60 mL of concentrated phosphoric acid.

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.S. *Modern Microcrystal Tests for Drugs*, Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

< 15 minutes

Crystal Morphology and Test Notes

Oily drops appear first, followed by nail- or clothespin-shaped crystals.

Photomicrograph of Typical Crystals

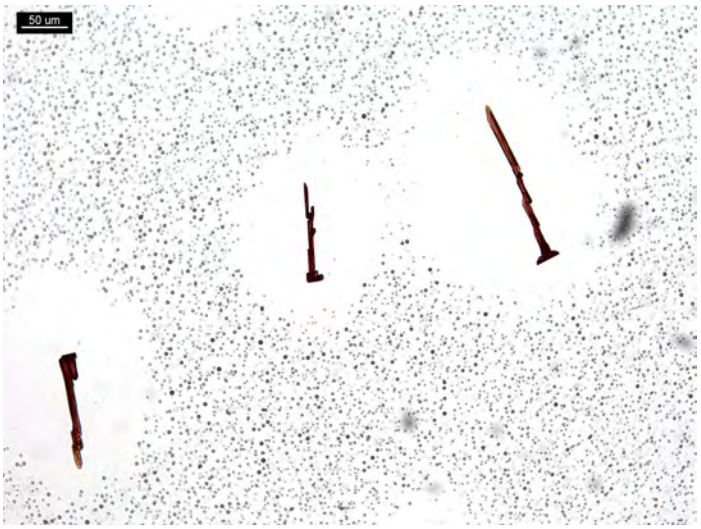


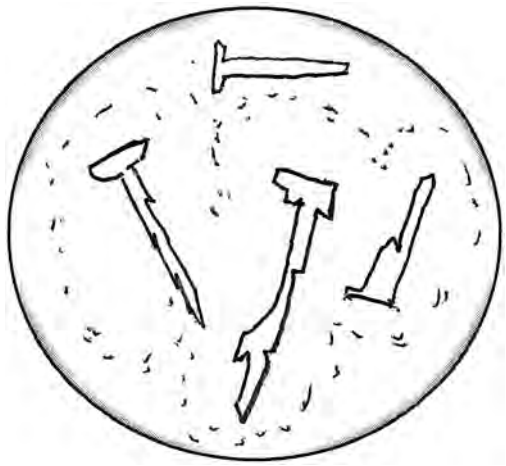
Figure 1. 1 PPP of *l*-ephedrine and 10 µL of the $HAuBr_4$ reagent. Crystals are nail-shaped.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on two pharmaceutical tablets: Bronkaid® (25 mg ephedrine sulfate and 400 mg guaifenesin) and Primatene® (12.5 mg ephedrine HCl and 200 mg guaifenesin). Because both tablets contain guaifenesin, which inhibits this microcrystal test, a chloroform extraction was required to remove the guaifenesin, which is soluble in chloroform; *l*-ephedrine is insoluble in chloroform. A portion of the tablet (≈ 3 mm x 3 mm x 3 mm) was placed in a microcentrifuge tube, several drops of chloroform were added and stirred with a pipette tip, then centrifuged. The chloroform was removed and discarded. The chloroform extraction can be repeated. A small amount of the remaining insoluble material was placed on a glass slide, and the direct test was performed. The chloroform extraction alone worked well with the Bronkaid®, however, the

Continued on following page

PLM Optical Properties

Approximate Size Range	5–10 µm width, 50–500 µm length
Color/Pleochroism	Red-orange; pleochroic dark red to orange or orange-yellow
Refractive Indices (RI)	n-parallel > 1.700 n-perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Crystals were gently heated then washed with RI liquid.
Estimated Birefringence	High
Extinction	Parallel, oblique and incomplete
Sign of Elongation	Positive (+) and negative (–). Crystals that are pleochroic red (parallel) and orange (perpendicular) have a positive sign of elongation. Crystals that are pleochroic orange (parallel) and red (perpendicular) have a negative sign of elongation.
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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l-Ephedrine: Gold Bromide (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

Primatene® tablet required an additional step: The remaining insoluble material was allowed to dry in the microcentrifuge tube, then two drops of water were added, the sample was stirred and mixed with a pipette tip, and centrifuged. 50 µl of the supernatant liquid was placed on a glass slide and allowed to dry with gentle heat, then the direct test was performed.

IR Spectrum

See Figure 15. Download SPC file.

Figure 2. 1 PPP of *l*-ephedrine and 10 µL of the $HAuBr_4$ reagent. Crystals are nail-shaped.

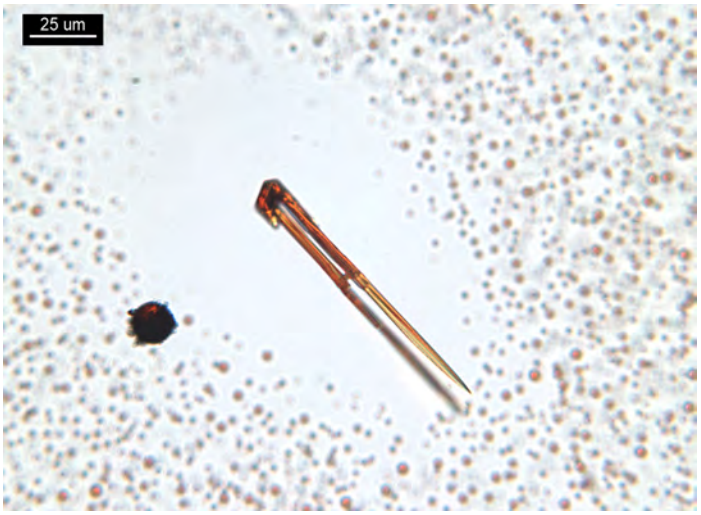

Figure 3. 1 PPP of *l*-ephedrine and 10 µL of the $HAuBr_4$ reagent. Crystals are clothespin-shaped.

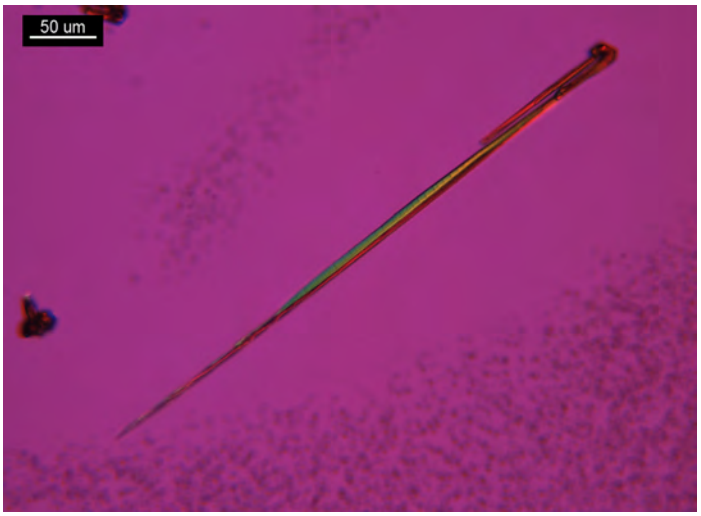

Figure 4. 1 PPP of *l*-ephedrine and 10 µL of the $HAuBr_4$ reagent. This nail-shaped crystal has a positive sign of elongation; crossed polars and Red I compensator.

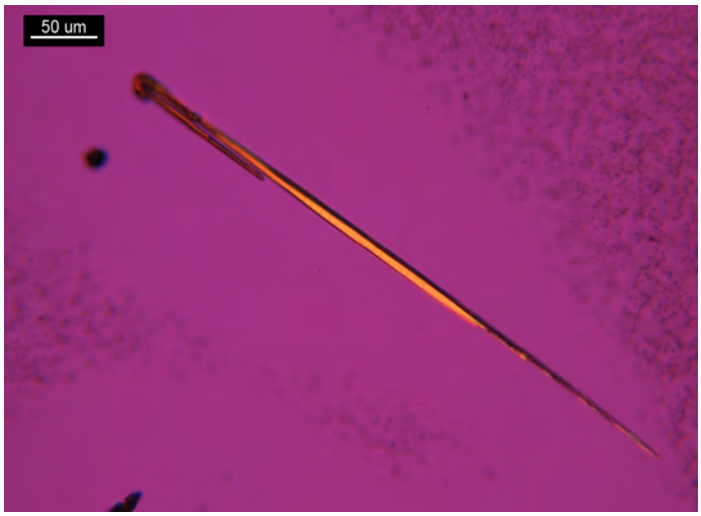

Figure 5. Same crystal as Figure 4. Crystal is rotated 90° counterclockwise. This nail-shaped crystal has a positive sign of elongation; crossed polars and Red I compensator.

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l-Ephedrine: Gold Bromide (continued)

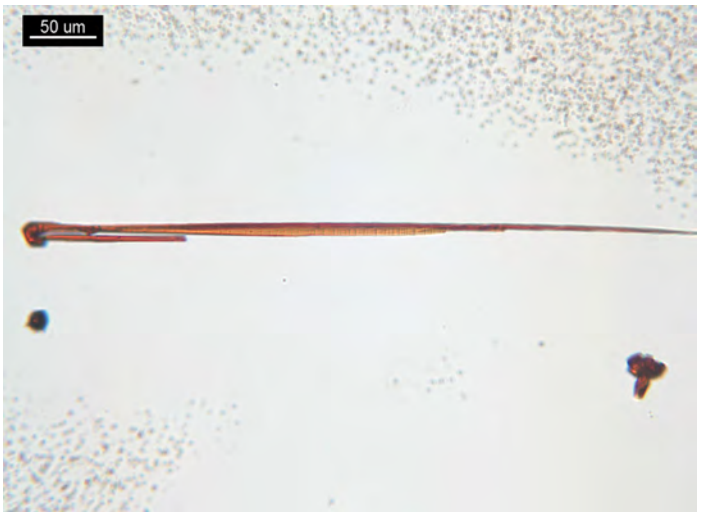

Figure 6. Same crystal as Figure 4. Microscope polarizer is oriented East-West. Note pleochroic dark red-orange color.

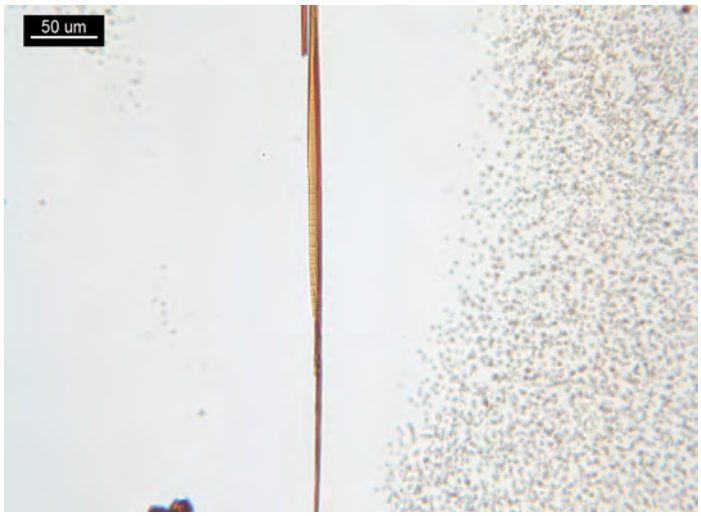

Figure 7. Same crystal as Figure 4. Microscope polarizer is East-West. Note pleochroic orange-yellow color.

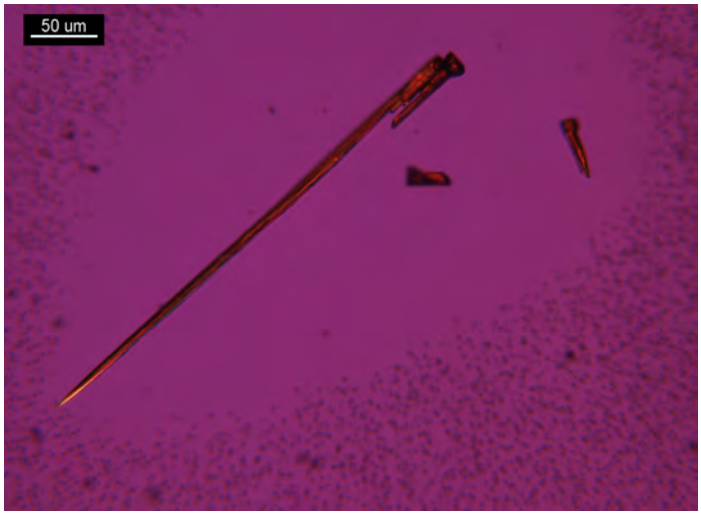

Figure 8. 1 PPP of *l*-ephedrine and 10 µL of the $HAuBr_4$ reagent. This nail-shaped crystal has a negative sign of elongation; crossed polars and Red I compensator.

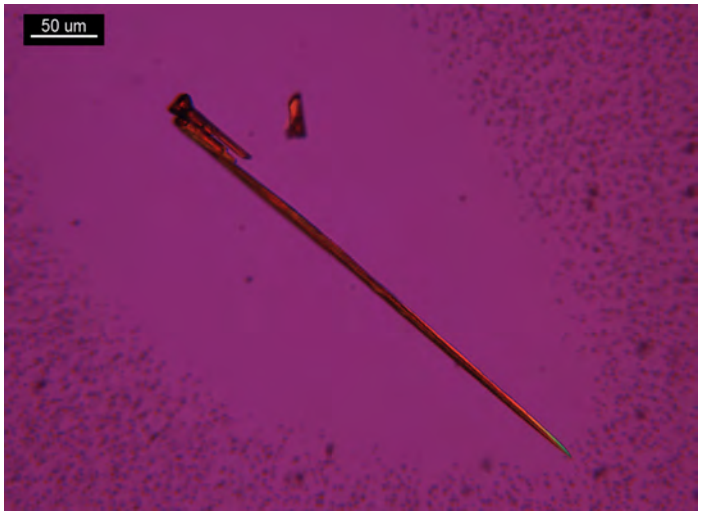

Figure 9. Same crystal as Figure 8. Crystal is rotated 90° counterclockwise. This nail-shaped crystal has a negative sign of elongation; crossed polars and Red I compensator.

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l-Ephedrine: Gold Bromide (continued)

Figure 10. Same crystal as Figure 8. Microscope polarizer is East-West. Note pleochroic orange color.

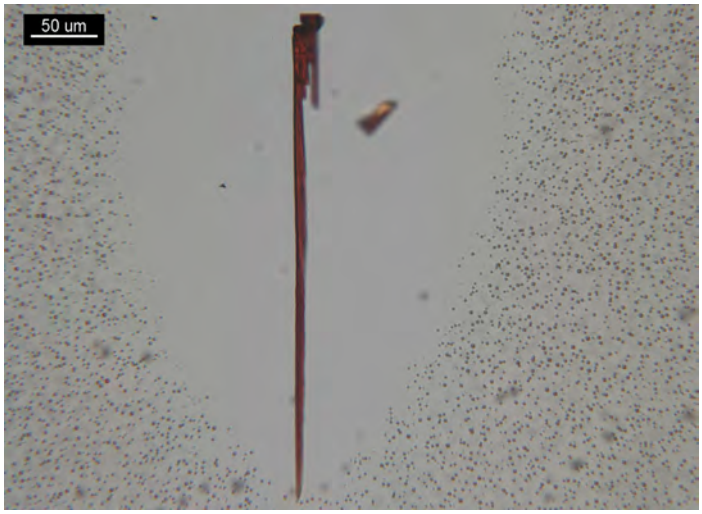

Figure 11. Same crystal as Figure 8. Microscope polarizer is oriented East-West. Note pleochroic red color.

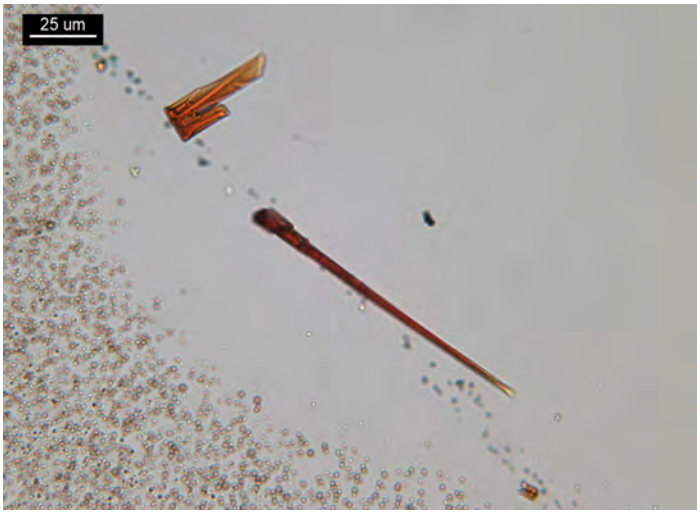

Figure 12. 1 PPP of insoluble material from a Bronkaid® (25 mg ephedrine sulfate and 400 mg guaifenesin) pharmaceutical tablet, after chloroform extraction to remove guaifenesin, and 10 µl of the $HAuBr_4$ reagent. Nail-shaped crystals formed within 15 minutes.

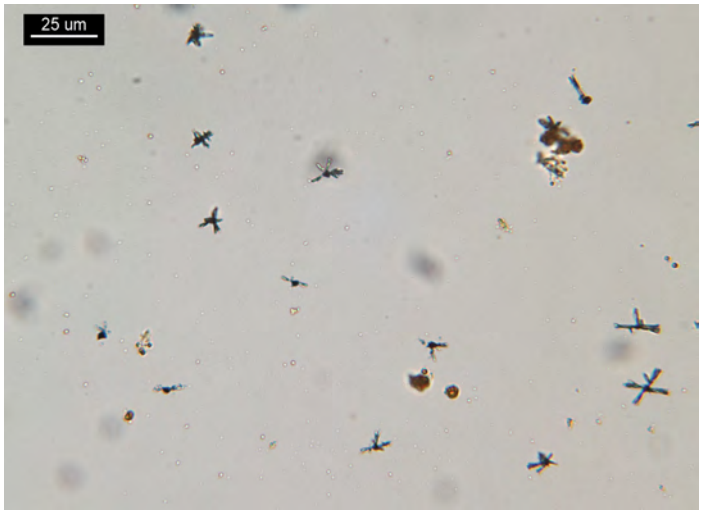

Figure 13. 1 PPP from a Bronkaid® (25 mg ephedrine sulfate and 400 mg guaifenesin) pharmaceutical tablet and 10 µL of the $HAuBr_4$ reagent; no chloroform extraction. Note guaifenesin and the gold bromide reagent formed star-shaped crystals within 15 minutes, but the typical nail-shaped crystals from ephedrine did not form.

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l-Ephedrine: Gold Bromide (continued)

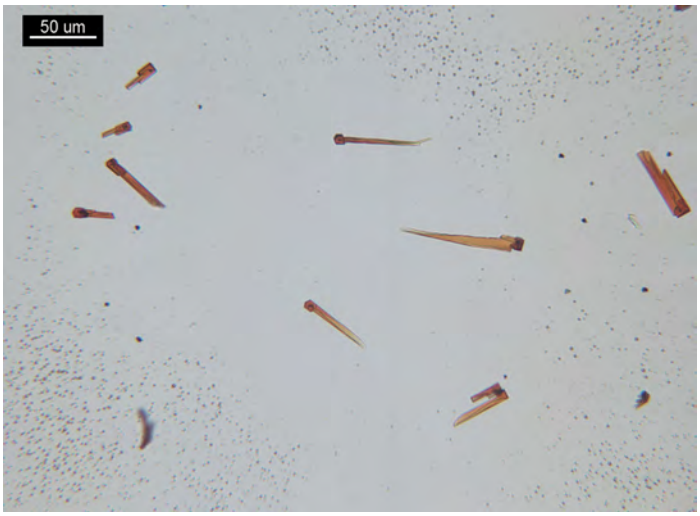

Figure 14. 50 µl of the supernatant liquid from a Primatene® (12.5 mg ephedrine HCl and 200 mg guaifenesin) pharmaceutical tablet. After the chloroform extraction to remove guaifenesin, the remaining insoluble material was allowed to dry in the microcentrifuge tube, two drops of water were added, then the sample was stirred and mixed with a pipette tip and centrifuged. 50 µl of the supernatant liquid was placed on a glass slide and allowed to dry with gentle heat, then 10 µl of the $HAuBr_4$ reagent was added. Nail- and clothespin-shaped crystals formed within 10 minutes.

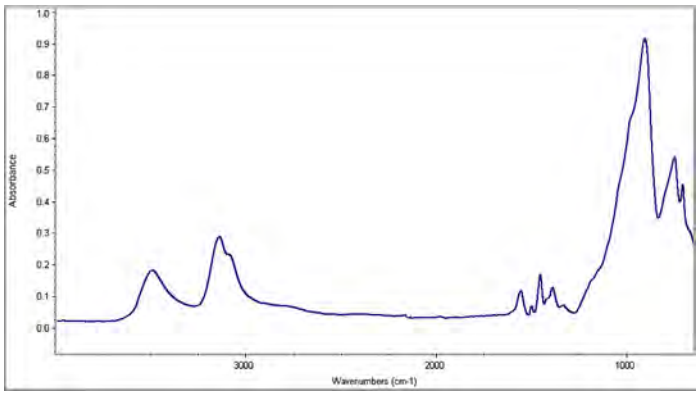

Figure 15. Infrared spectrum of *l*-ephedrine gold bromide precipitate. Download SPC file.

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l-Ephedrine: Gold Chloride

REAGENT 2: Gold Chloride ($HAuCl_4$)

1 g of $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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: Add 5 µL of reagent directly to the sample; no coverslip.

References

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

Limit of Detection

1 PPP

Time Required for Crystal Formation

15 minutes

Crystal Morphology and Test Notes

Oily drops appear first (usually < 1 minute), followed by crystals that appear as elongated plates, which are stepped and jointed at 90°.

Photomicrograph of Typical Crystals

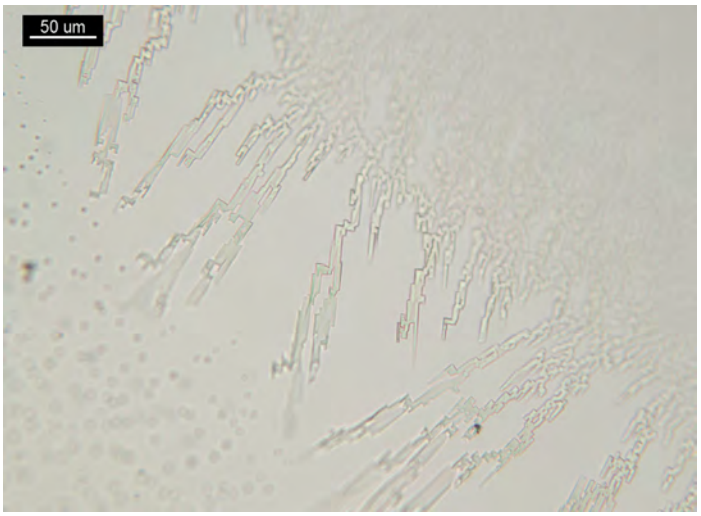


Figure 1. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Crystals form elongated plates that are stepped and jointed at 90°.

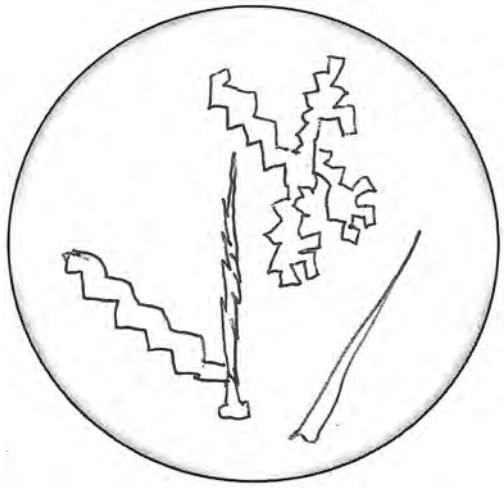
Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on two pharmaceutical tablets: Bronkaid® (25 mg ephedrine sulfate and 400 mg guaifenesin) and Primatene® (12.5 mg ephedrine HCl and 200 mg guaifenesin). Because both tablets contain guaifenesin, which inhibits this microcrystal test, a chloroform extraction was required to remove the guaifenesin, which is soluble in chloroform; *l*-ephedrine is insoluble in chloroform. A portion of the tablet (≈ 3 mm x 3 mm x 3 mm) was placed in a microcentrifuge tube, several drops of chloroform were added and stirred with a pipette tip, then centrifuged. The chloroform was removed and discarded. The chloroform extraction can be repeated. A small amount of the remaining insoluble material was placed on a glass slide, and the direct test was performed.

PLM Optical Properties

Approximate Size Range	> 10 µm width, > 300 µm length
Color/Pleochroism	Pale yellow; 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	Crystals were gently heated then washed with RI liquid.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 17. Download SPC file.

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l-Ephedrine: Gold Chloride (continued)

Figure 2. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Oily drops form immediately after adding the reagent.

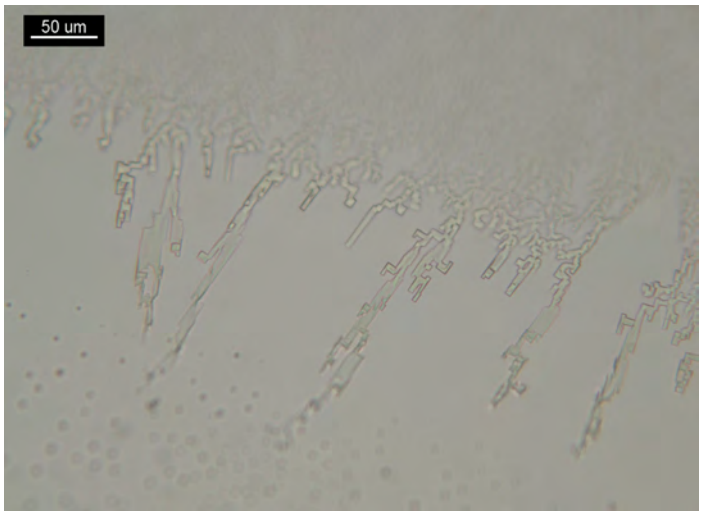

Figure 3. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Crystals form elongated plates that are stepped and jointed at 90°.

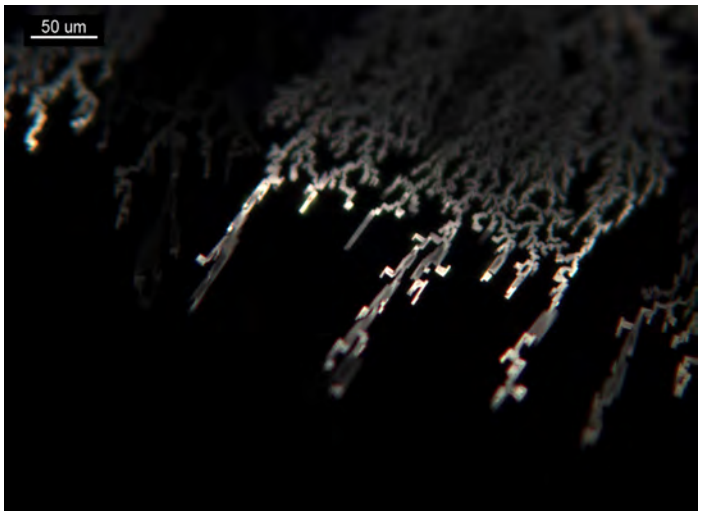

Figure 4. Same as Figure 3; crossed polars.

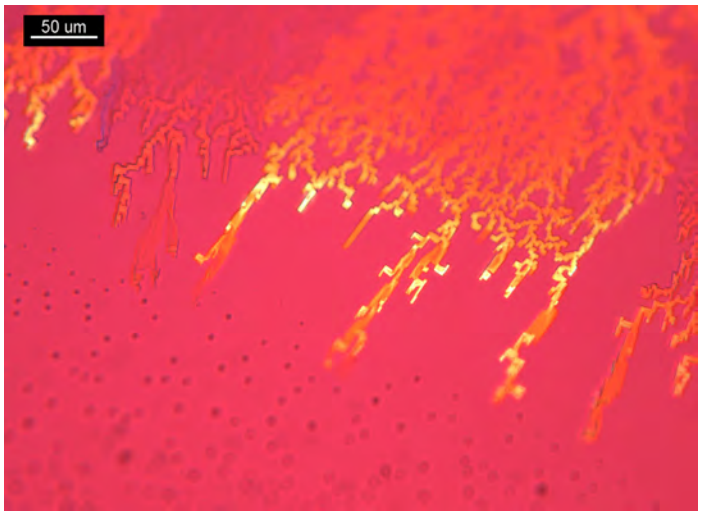

Figure 5. Same as Figure 3; crossed polars and Red I compensator.

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l-Ephedrine: Gold Chloride (continued)

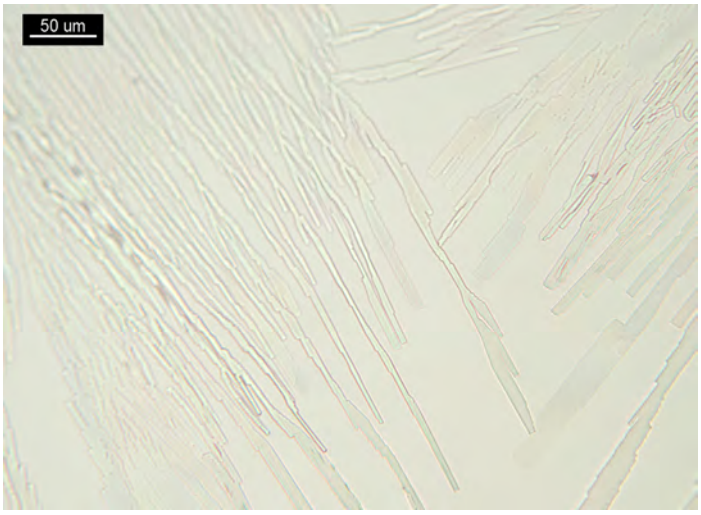

Figure 6. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Crystals form elongated plates that are stepped and jointed at 90°.

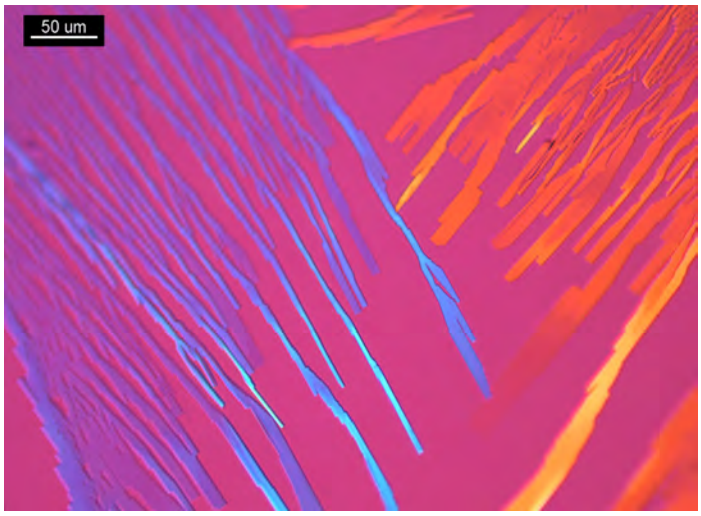

Figure 7. Same as Figure 6. Elongated plates that are stepped and jointed have a negative sign of elongation; crossed polars and Red I compensator.

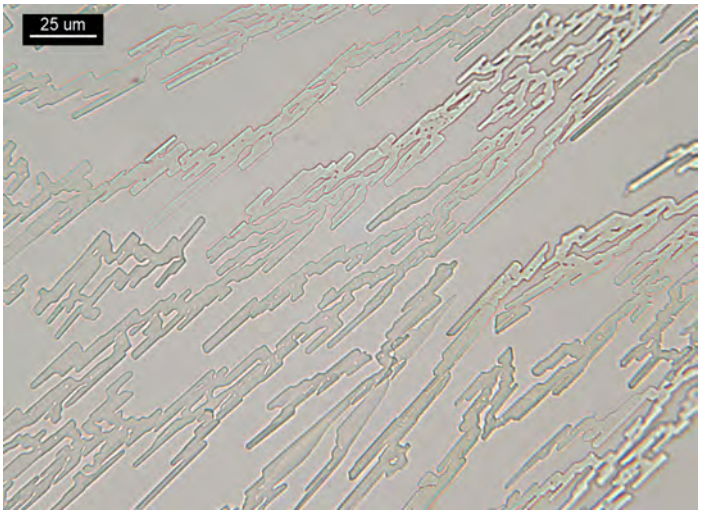

Figure 8. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Crystals form elongated plates that are stepped and jointed at 90°.

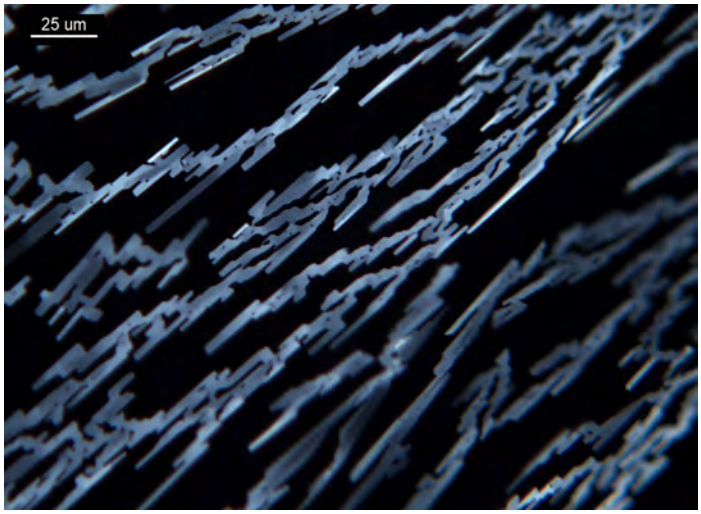

Figure 9. Same as Figure 8; crossed polars.

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l-Ephedrine: Gold Chloride (continued)

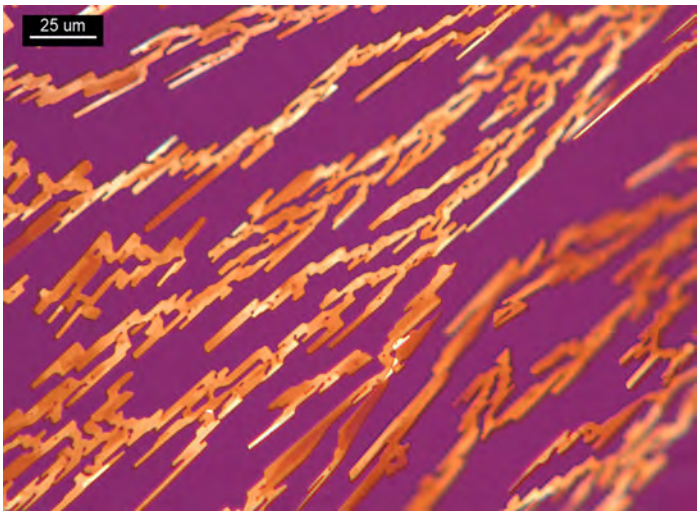

Figure 10. Same as Figure 8. Elongated plates that are stepped and jointed have a negative sign of elongation; crossed polars and Red I compensator.

Figure 11. 1 PPP of *l*-ephedrine and 5 µL of $HAuCl_4$ reagent. Note parallel extinction: Vibration directions are parallel and perpendicular to the long direction of the crystal faces; crossed polars and Red I compensator.

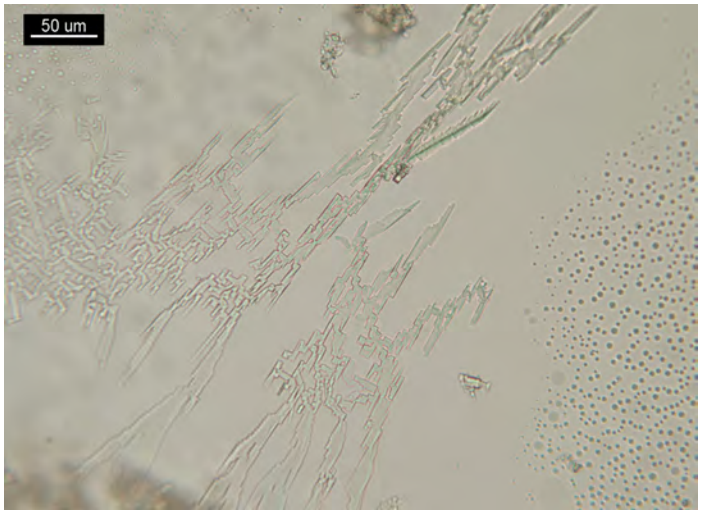

Figure 12. 1 PPP of insoluble material and 5 µL of $HAuCl_4$ reagent after chloroform extraction to remove guaifenesin from a Bronkaid® pharmaceutical tablet (25 mg ephedrine and 400 mg guaifenesin). Crystals form elongated plates that are stepped and jointed at 90°.

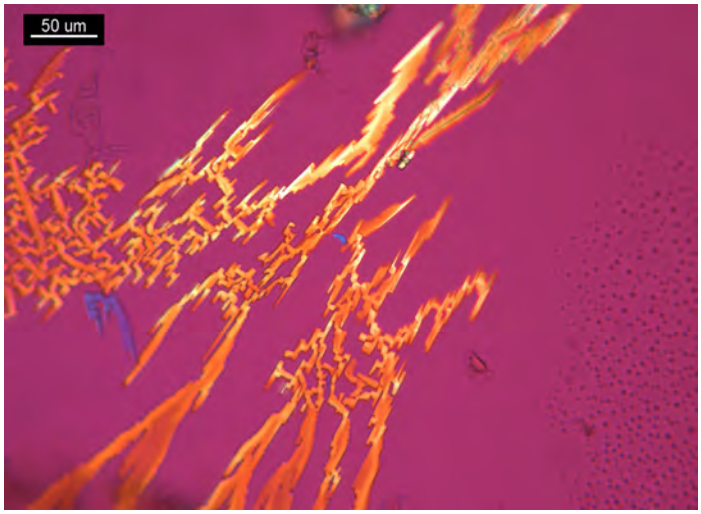

Figure 13. Same as Figure 12; crossed polars and Red I compensator.

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l-Ephedrine: Gold Chloride (continued)

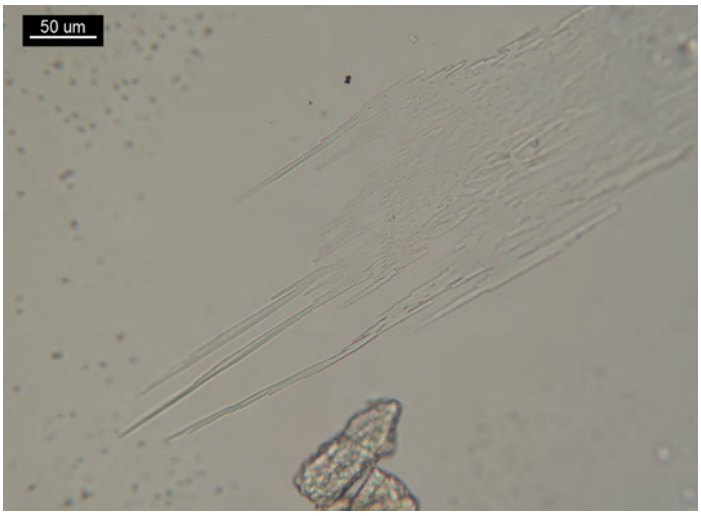

Figure 14. 1 PPP of insoluble material and 5 µL of $HAuCl_4$ reagent after chloroform extraction to remove guaifenesin from a Primatene® pharmaceutical tablet (12.5 mg ephedrine and 200 mg guaifenesin). Crystals form elongated plates that are stepped and jointed at 90°.

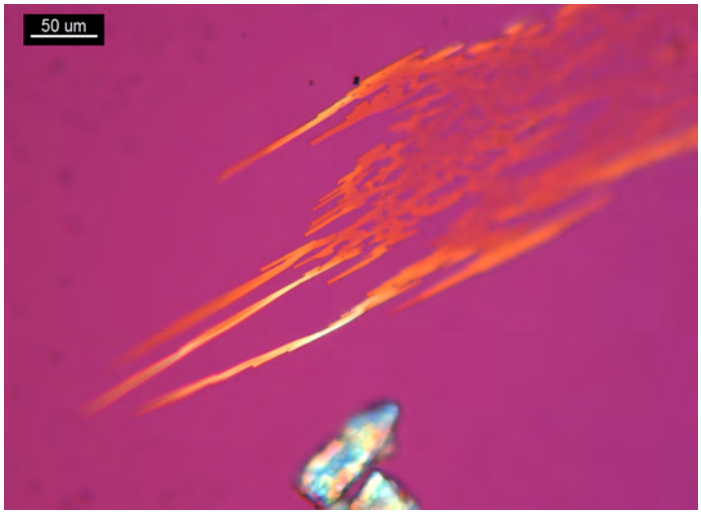

Figure 15. Same as Figure 14; crossed polars and Red I compensator.

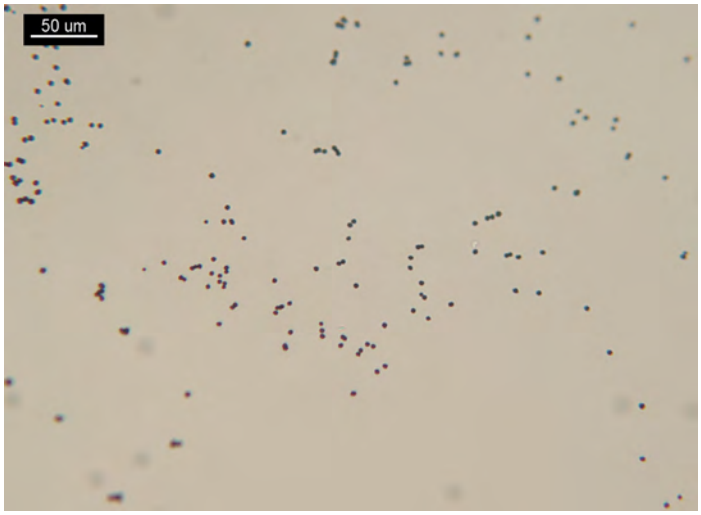

Figure 16. 1 PPP of guaifenesin (no *l*-ephedrine) and 5 µL of $HAuCl_4$ reagent. Crystals form numerous opaque or pseudo-opaque particles, which are black in transmitted light and shiny gold in reflected light, formed in ≈ 15 minutes.

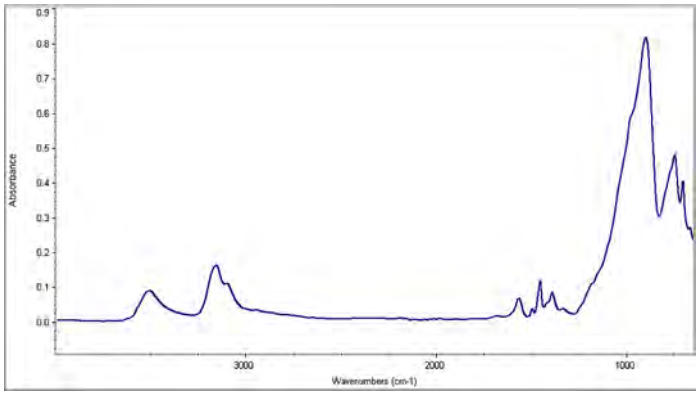

Figure 17. Infrared spectrum of *l*-ephedrine gold chloride precipitate. Download SPC file.

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Heroin: Mercuric Chloride

REAGENT 1: Mercuric Chloride ($HgCl_2$)

5% aqueous: 1 g $HgCl_2$ in H_2O, make up to 20 mL. Reagent needs to be gently warmed to get mercuric chloride into solution.

Test Method

Direct test: Dissolve sample in 5 µL of 1% HCl. Reagent drop is added directly to the test drop; no coverslip.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.
2. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate. Some adulterated samples may take up to 10 min.

Crystal Morphology and Test Notes

Small burrs and seed crystals develop into large branched, feathery and curved dendrites, needles, blades and straight plates.

Photomicrograph of Typical Crystals

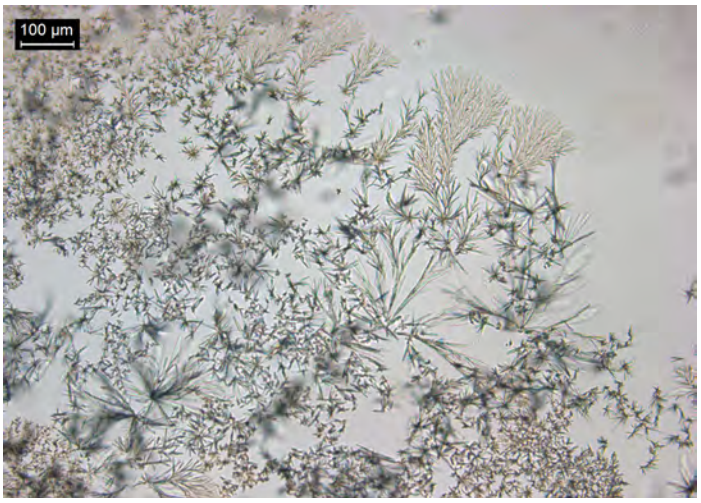

Figure 1. 1 PPP of heroin in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form dendritic needles that become branched and feathery over time.

Pharmaceuticals, Adulterants or Other Drug Interactions

Common adulterants with heroin that may inhibit or distort crystal formation include acetaminophen, caffeine, clenbuterol, phenobarbitol, procaine, quinine, scopolamine and strychnine. The detectability of heroin with selected adulterants is listed below:

- Acetaminophen:heroin – detectable at 1:5, 1:1 and 5:1
- Caffeine:heroin – detectable at 1:5, 1:1 and 5:1
- Clenbuterol:heroin –detectable at 1:5, 1:1 and 5:1
- Phenobarbitol:heroin – detectable at 1:5, 1:1 and 5:1
- Procaine:heroin – detectable at 1:5 and 1:1; detectable with distortions at 5:1
- Quinine:heroin – detectable at 1:5 and 1:1; detectable with distortions at 5:1
- Scopolamine:heroin – detectable with distortions at 1:5, 1:1 and 5:1
- Strychnine:heroin – detectable at 1:5; detectable with distortions at 1:1; undetectable at 5:1

PLM Optical Properties

Approximate Size Range	3–5 µm seed crystals, 10 µm to > 100 µm burrs; blades and needles 1 µm or longer.
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel ≈ 1.600 n-perpendicular ≈ 1.640

Morphology Illustration

not to scale

How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature then washed with ethanol (some crystals dissolved).
Estimated Birefringence	Moderate–High
Extinction	Oblique
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 12. Download SPC file.

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Heroin: Mercuric Chloride (continued)

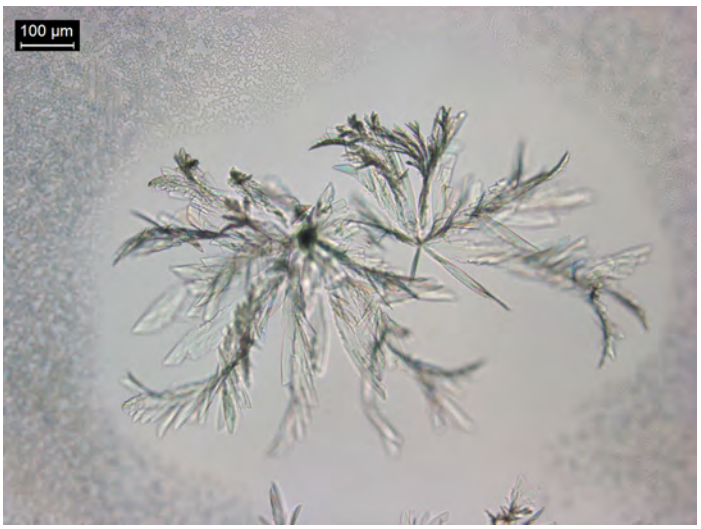

Figure 2. 1 PPP of heroin in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form feathery dendrites.

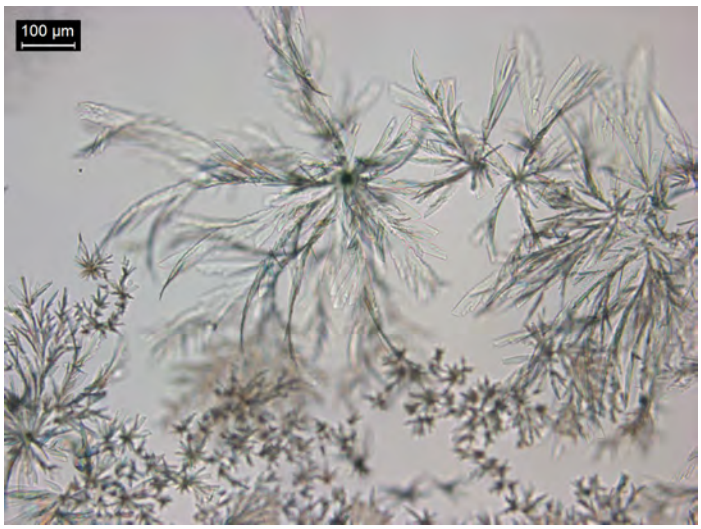

Figure 3. 1 PPP of heroin in 5 µL of 1% HCl and 5 µL of $HgCl_2$. reagent. Crystals form feathery dendrites.

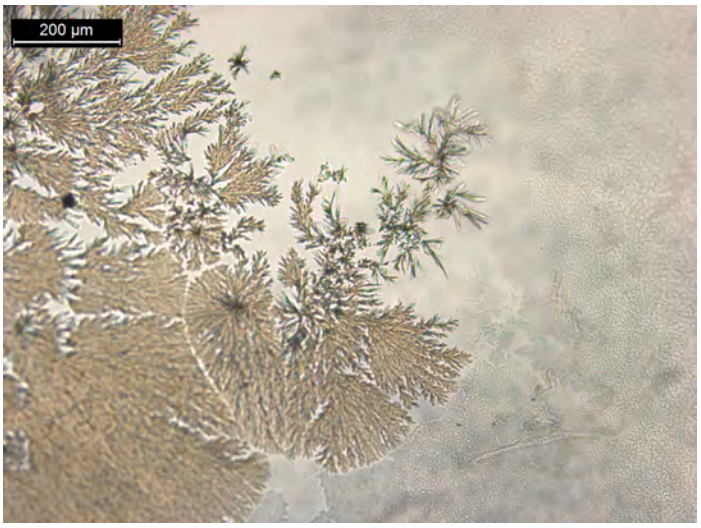

Figure 4. Acetaminophen:heroin, 1:5 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form feathery dendrites.

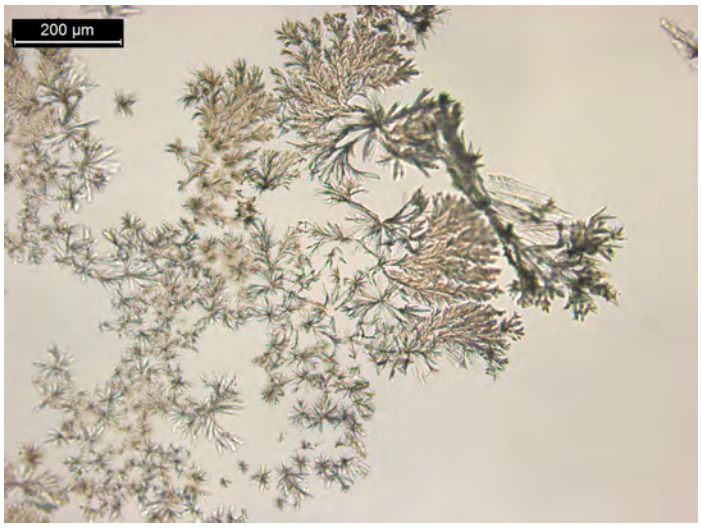

Figure 5. Caffeine:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form feathery dendrites.

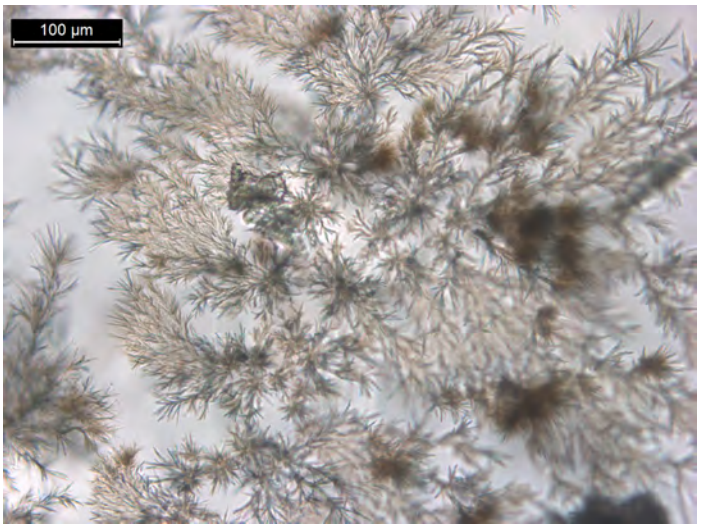

Figure 6. Clenbuterol:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form feathery dendrites.

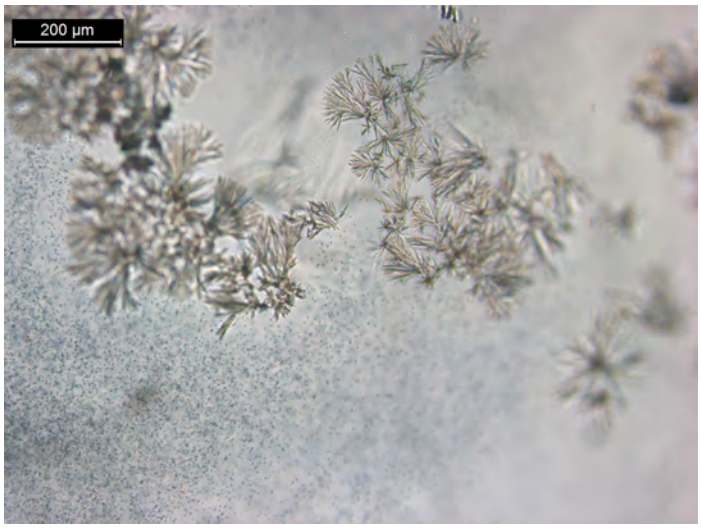

Figure 7. Phenobarbitol:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form feathery dendrites.

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Heroin: Mercuric Chloride (continued)

Figure 8. Procaine:heroin, 5:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form dendrites.

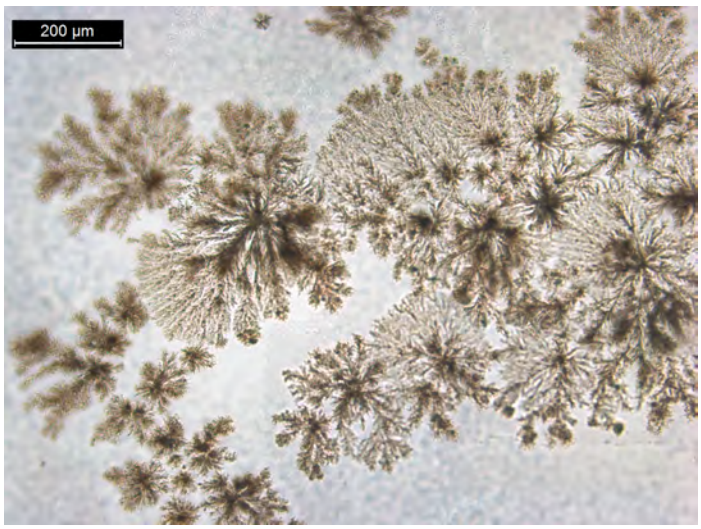

Figure 9. Quinine:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form dendrites.

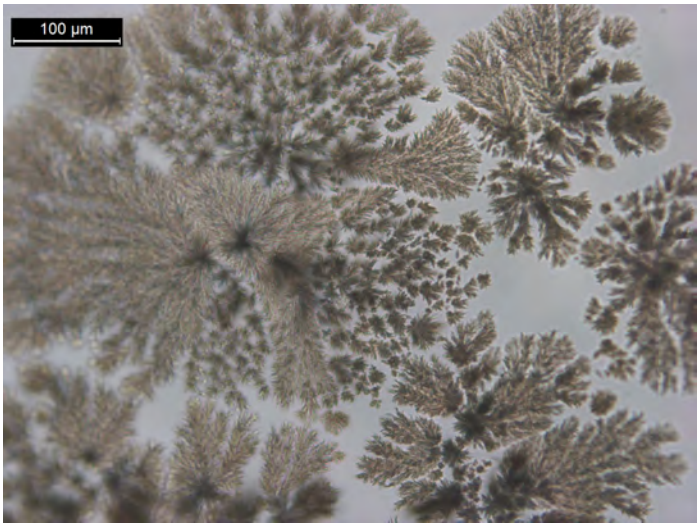

Figure 10. Scopolamine:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystals form distorted dendrites.

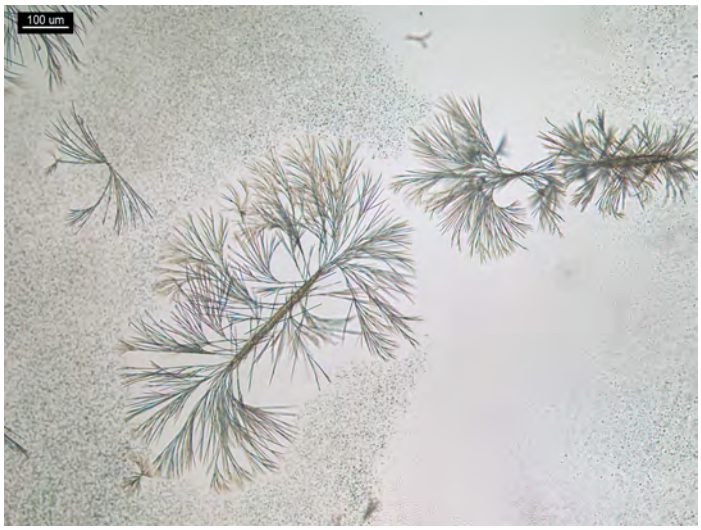

Figure 11. Strychnine:heroin, 1:1 in 5 µL of 1% HCl and 5 µL of $HgCl_2$ reagent. Crystal form distorted dendrites.

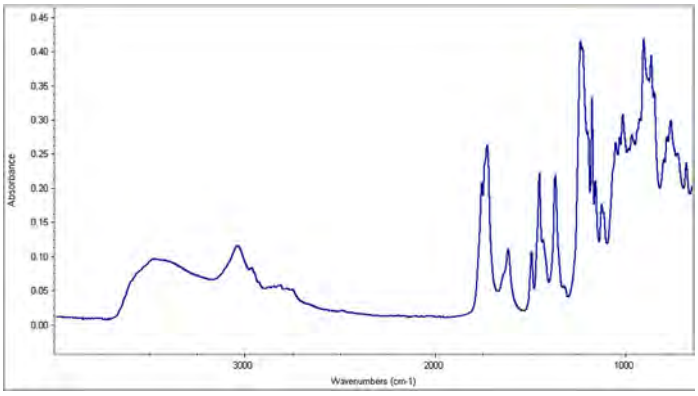

Figure 12. Infrared spectrum of heroin mercuric chloride precipitate. Download SPC file.

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Heroin: Mercuric Iodide

REAGENT 2: Mercuric Iodide (HgI_2)

1 g HgI_2 saturated in 20 mL (27+73) HCl. Note: (27+73) HCl is dilute hydrochloric acid made by combining 27 mL of concentrated hydrochloric acid with 73 mL of water.

Test Method

Direct test: Add 5 µL of reagent directly to sample on a glass slide. Swirl the drop two to three times with a pipette tip or glass rod; no coverslip.

References

1. Fulton, C.S. *Modern Microcrystal Tests for Drugs*, Wiley-Interscience: New York, 1969.
2. Kilbourn, J. "Microcrystal Analysis" for Florida Department of Law Enforcement workshop on Microscopy of Drugs, March 1988.
3. Wielbo, D. and Tebbett, I. "The Use of Microcrystal Tests in Conjunction with Fourier Transform Infra Red Spectroscopy for the Rapid Identification of Street Drugs," *Journal of Forensic Sciences*, 37:4, July 1992.

Limit of Detection

2 PPP

Time Required for Crystal Formation

≈ 2 minutes

Crystal Morphology and Test Notes

Straight-branched and forked dendrites, needles, fans, branched paddles and blades. Heroin base with this reagent forms curved and wispy needles with broom-like ends. 3–5 µm seed crystals grow first.

Photomicrograph of Typical Crystals

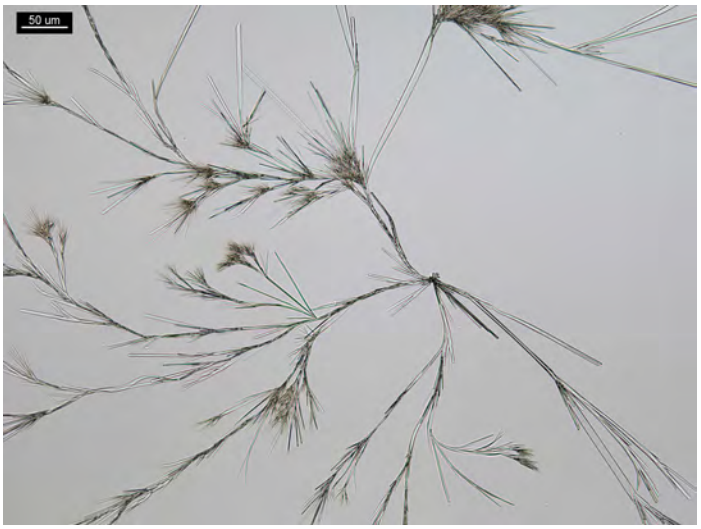


Figure 1. 2 PPP of heroin and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, needles and branched paddles.

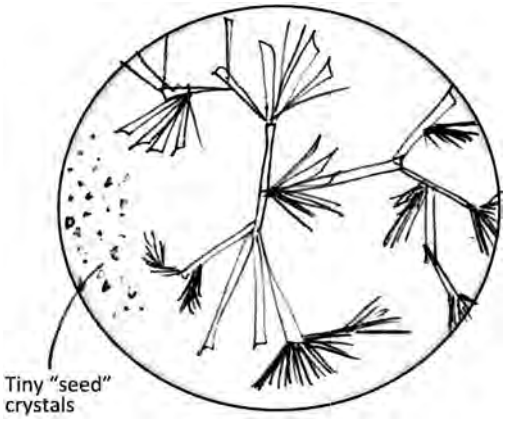
Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on heroin in the presence of acetaminophen, caffeine, clenbuterol, phenobarbitol, procaine, quinine, scopolamine and strychnine and had no effect on the resulting crystals.

IR Spectrum

See Figure 13. Download SPC file.

PLM Optical Properties

Approximate Size Range	10 µm to > 100 µm; needles 1 µm or longer
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel ≈ 1.690 n_1-perpendicular ≈ 1.690 n_2-perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Crystals were gently heated.
Estimated Birefringence	Moderate–High
Extinction	Parallel; anomalous first-order gray interference colors appear blue.
Sign of Elongation	Positive (+) and negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Heroin: Mercuric Iodide (continued)

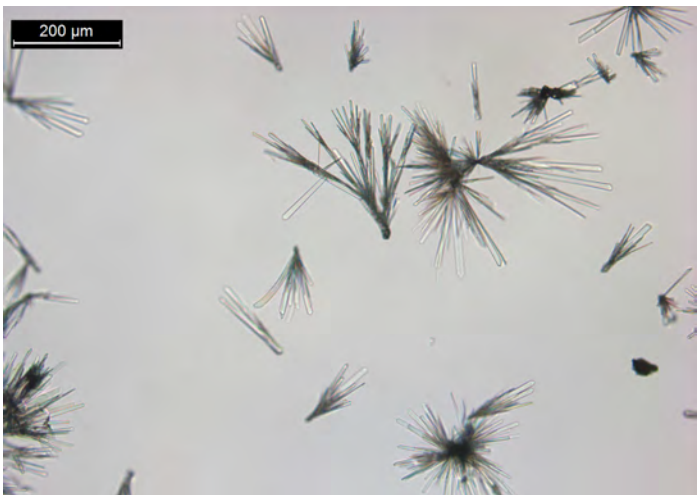

Figure 2. Acetaminophen:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, and fans.

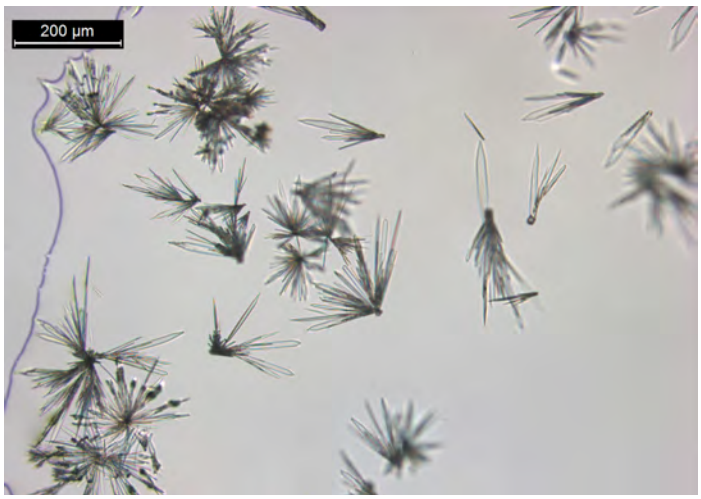

Figure 3. Caffeine:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, and fans.

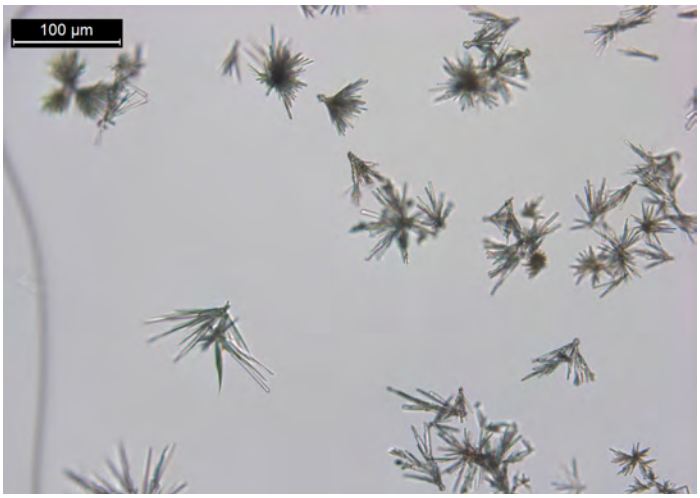

Figure 4. Clenbuterol:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, and fans.

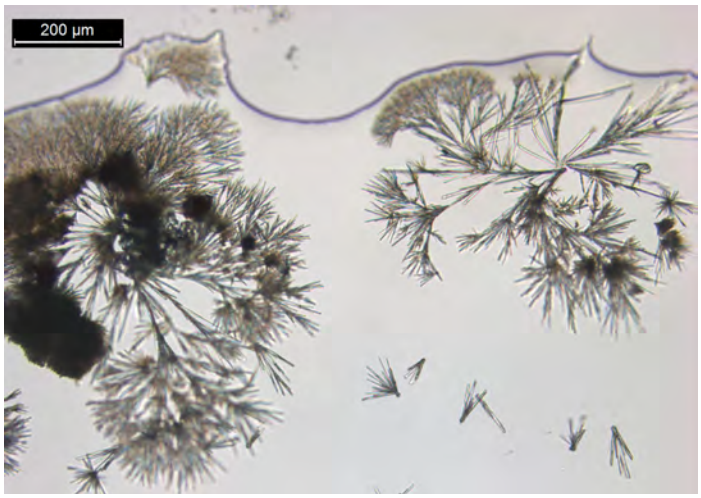

Figure 5. Phenobaritol:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, and fans.

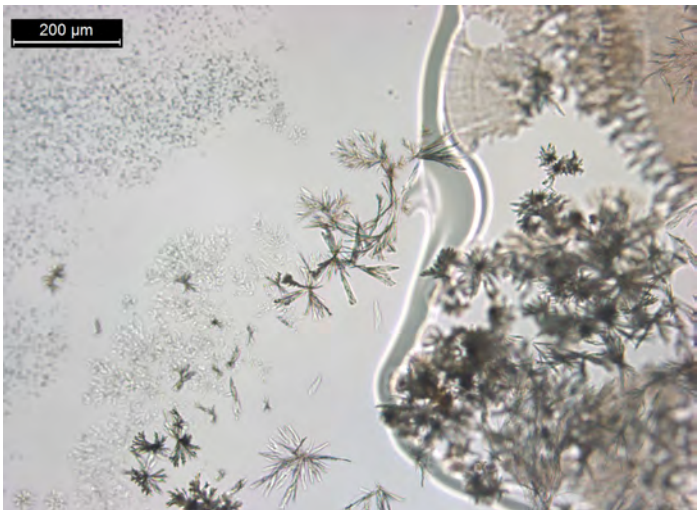

Figure 6. Procaine:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, and fans.

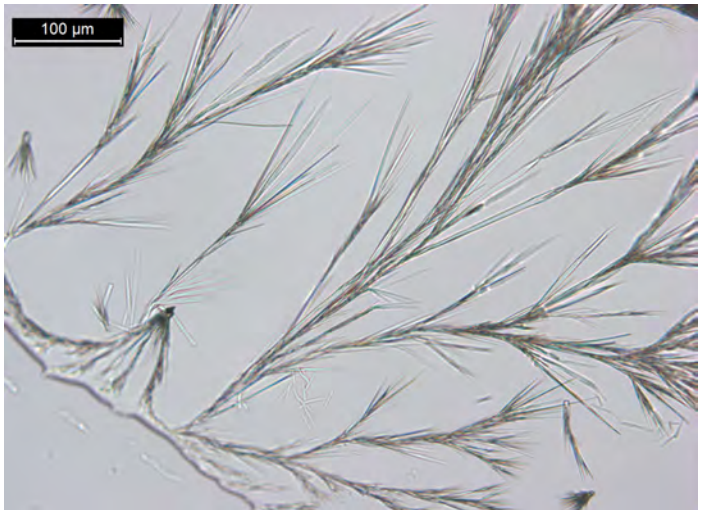

Figure 7. Quinine:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, needles and branched paddles.

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Heroin: Mercuric Iodide (continued)

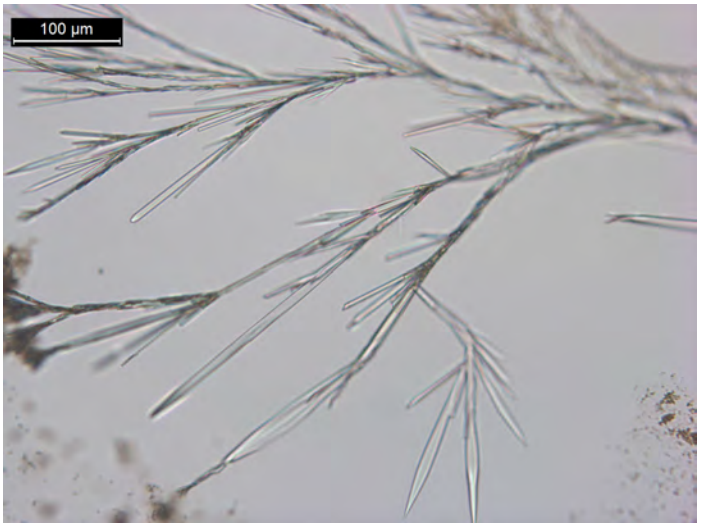

Figure 8. Scopolamine:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, needles and branched paddles.

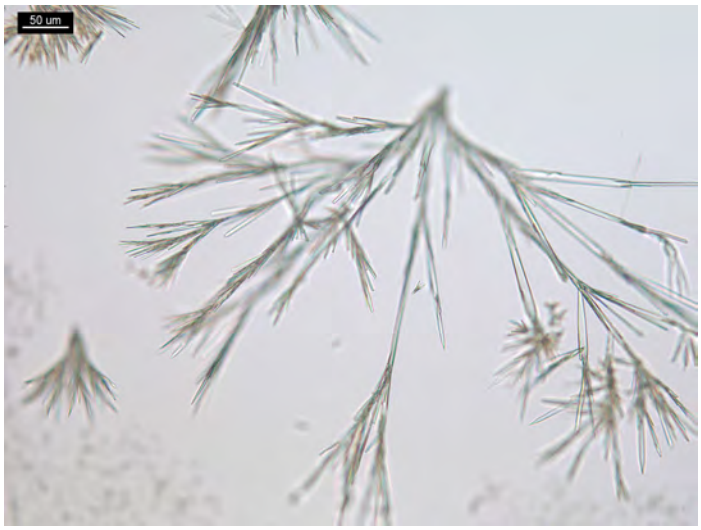

Figure 9. Strychnine:heroin, 1:1 and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form straight-branched and forked dendrites, needles and branched paddles.

Figure 10. Heroin base and 5 µL of HgI_2 and (27+73) HCl reagent. Crystals form curvy, wispy needles, arranged like broomsticks.

Figure 11. 2 PPP of heroin and 5 µL of HgI_2 and (27+73) HCl reagent. Anomalous first-order gray interference colors appear blue; crossed polars.

Figure 12. Same as Figure 11; crossed polars and Red I compensator.

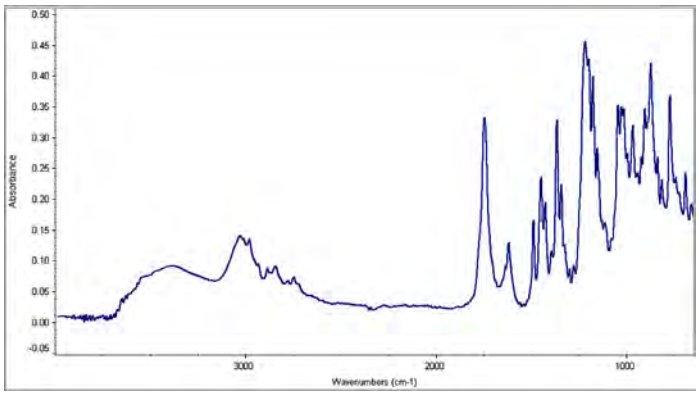

Figure 13. Infrared spectrum of heroin mercuric iodide precipitate. Download SPC file.

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Hydrocodone: Platinum Bromide

REAGENT: Platinum Bromide (H_2PtBr_6)

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. (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.

Test Method

Direct test: Dissolve sample in 5 µL of water, then add 5 µL of reagent. Mix with a pipette tip, glass rod or toothpick.

References

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

Limit of Detection

1 PPP

Time Required for Crystal Formation

< 1 minute

Crystal Morphology and Test Notes

Clusters of yellow-brown precipitates form quickly and turn into rosettes of fine needles.

Photomicrograph of Typical Crystals

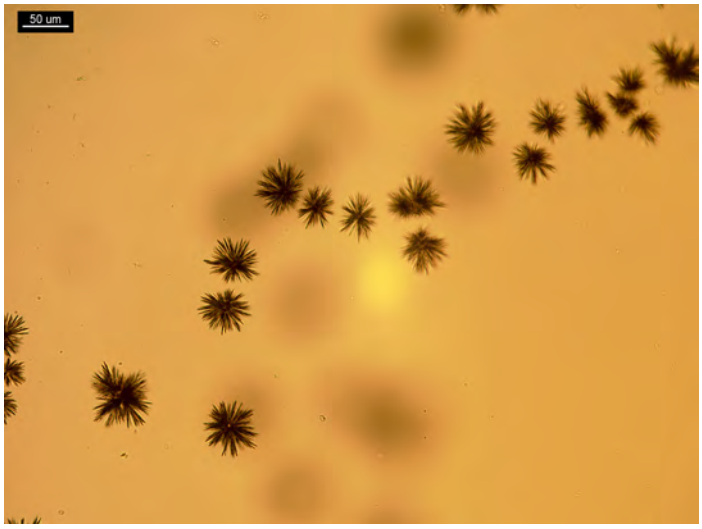


Figure 1. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form rosettes of needles.

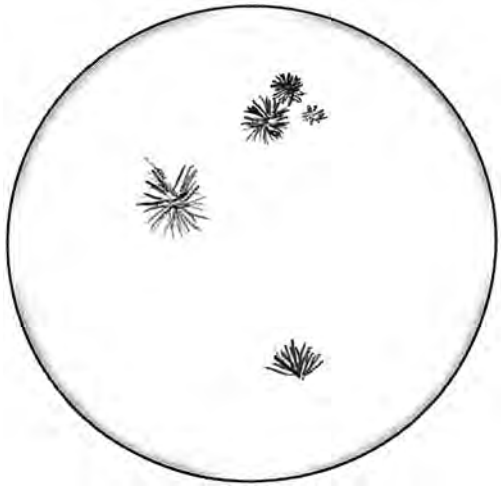
Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 mg and 10 mg tablets containing hydrocodone and acetaminophen after an extraction procedure to remove the acetaminophen was performed: 10–15 mg from the inner portion of the tablet was removed with a clean razor and placed into a microcentrifuge tube. The following were added in the microcentrifuge tube and shaken after each addition: 200 µL of water, 200 µL of saturated aqueous sodium bicarbonate, and 50 µL of chloroform. After separation of the phases, 5 µL from the chloroform layer was transferred to a glass slide, dried and tested directly. This test was unsuccessful on oral solutions that contained hydrocodone (e.g. cough syrup with hydrocodone) even after multiple extraction procedures were performed.

PLM Optical Properties

Approximate Size Range	Rosettes: 20 to > 30 µm Individual needles: 1 µm width
Color/Pleochroism	Yellow-brown; not pleochroic
Refractive Indices (RI)	n > 1.700

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then washed with absolute ethanol.
Estimated Birefringence	High
Extinction	Undulose
Sign of Elongation	Negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 15. Download SPC file.

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Hydrocodone: Platinum Bromide (continued)

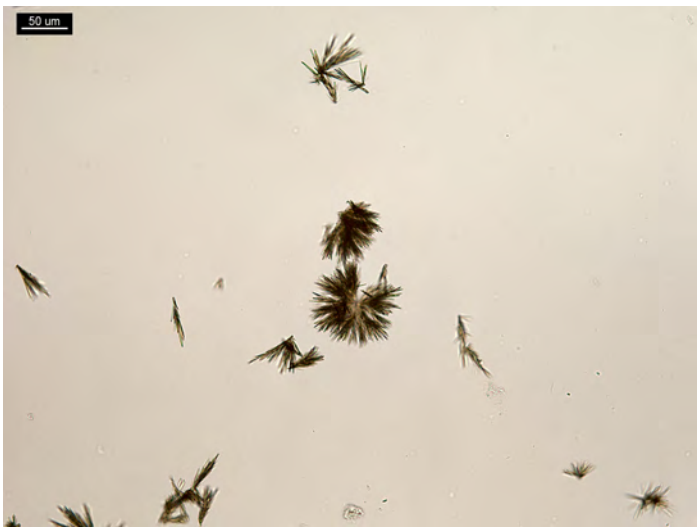

Figure 2. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form rosettes and broken rosettes.

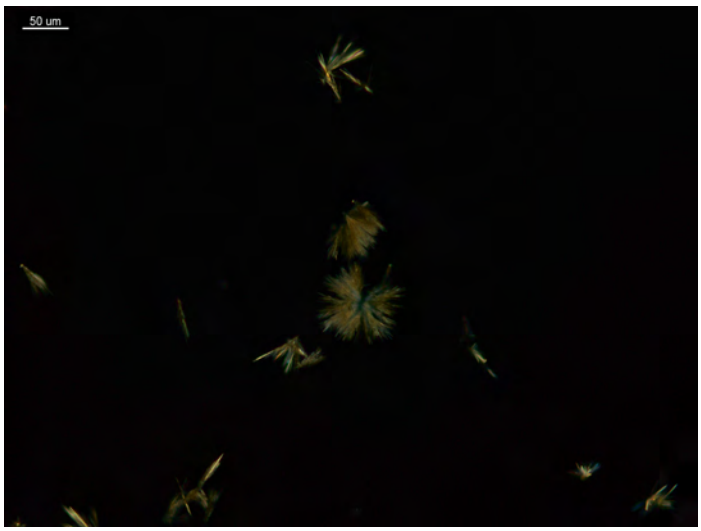

Figure 3. Same as Figure 2; crossed polars.

Figure 4. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form rosettes and broken rosettes. Needles have a negative sign of elongation; crossed polars and Red I compensator.

Figure 5. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form rosettes and broken rosettes. Needles have a negative sign of elongation; crossed polars and Red I compensator.

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Hydrocodone: Platinum Bromide (continued)

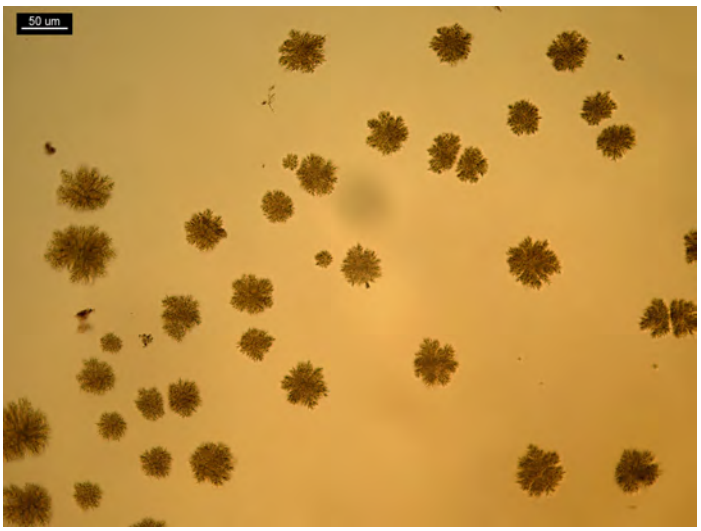

Figure 6. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form rosettes of needles in a hanging drop.

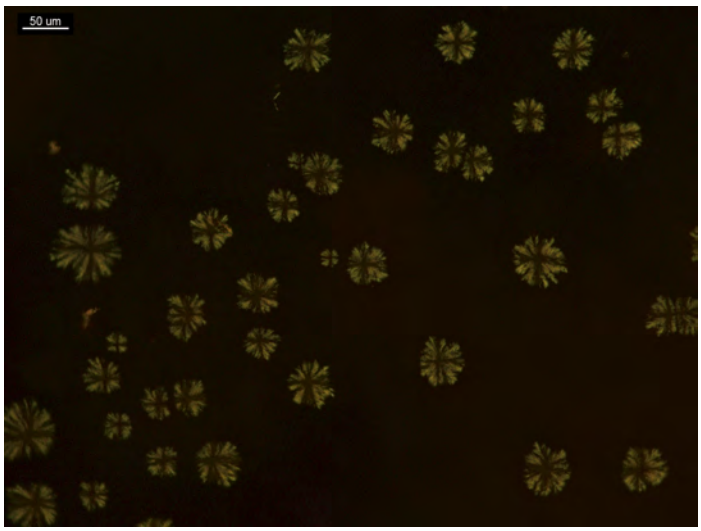

Figure 7. Same as Figure 6; crossed polars.

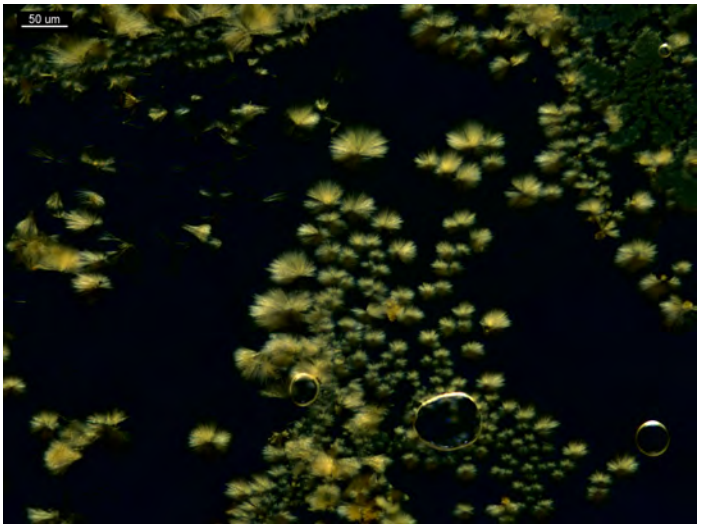

Figure 8. 1 PPP of hydrocodone in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form yellow rosettes of needles; reflected light.

Figure 9. 1 PPP of acetaminophen (no hydrocodone) in 5 µL of water and 5 µL of reagent mixture: H_2PtBr_6, HBr, and (2+3) H_2SO_4. Crystals form yellow blades and sheaves.

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Hydrocodone: Platinum Bromide (continued)

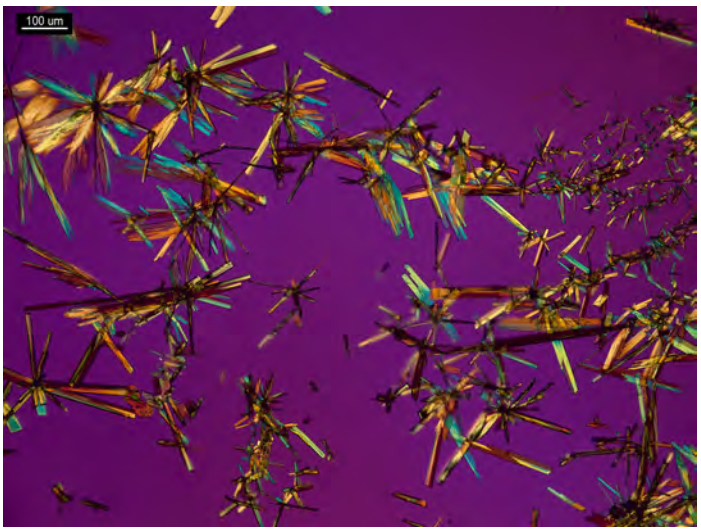

Figure 10. Same as Figure 9. Yellow blades and sheaves have a negative sign of elongation; crossed polars and Red I compensator.

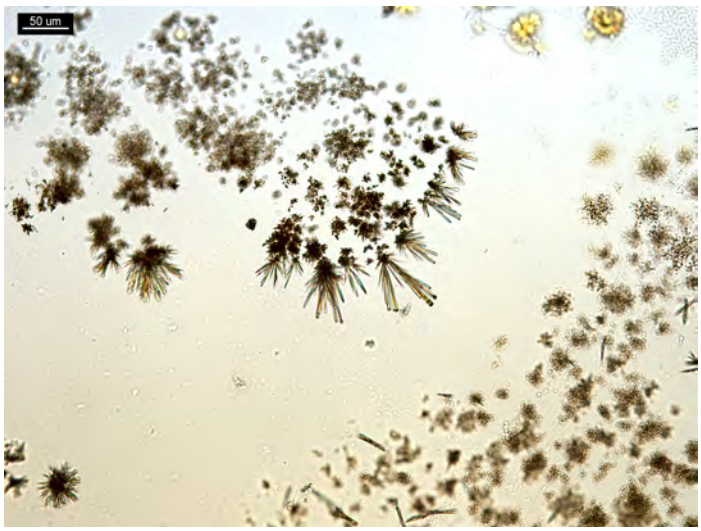

Figure 11. 10 mg hydrocodone and 325 mg acetaminophen tablet in 5 µL of water and 5 µL of reagent mixture, after extraction procedure. Clusters of yellow-brown precipitates form quickly and turn into rosettes of fine needles.

Figure 12. Same as Figure 11. Rosettes of fine needles have a negative sign of elongation; crossed polars and Red I compensator.

Figure 13. 5 mg hydrocodone and 500 mg acetaminophen tablet in 5 µL of water and 5 µL of reagent mixture, after extraction procedure. Clusters of yellow-brown precipitates form quickly and turn into rosettes of fine needles.

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Hydrocodone: Platinum Bromide (continued)

Figure 14. 5 mg hydrocodone and 500 mg acetaminophen tablet in 5 µL of water and 5 µL of reagent mixture, after extraction procedure. Clusters of yellow-brown precipitates form quickly and turn into rosettes of fine needles.

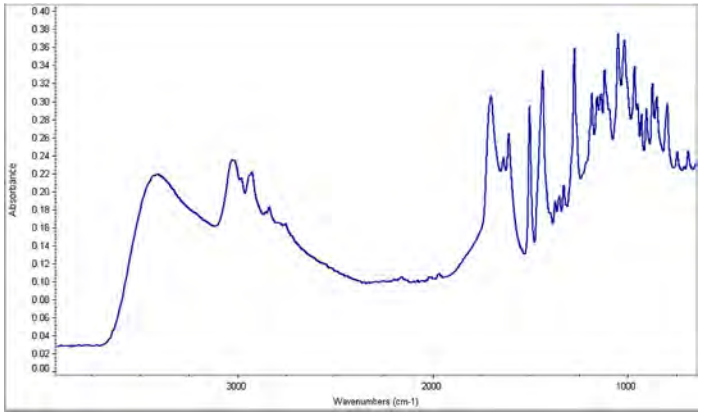

Figure 15. Infrared spectrum of hydrocodone platinum bromide precipitate. Download SPC file.

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Hydromorphone: Platinum Bromide

REAGENT 1: Platinum Bromide (H_2PtBr_6)

Three solutions are mixed together immediately prior to testing: **Solution 1:** 1.3 g H_2PtBr_6 in H_2O, make up to 20 mL. Alternatively, to convert platinum chloride to platinum bromide: 1 g $H_2PtCl_6 \cdot 6H_2O$ + 1.7 mL HBr (40%) in H_2O, make up to 20 mL. **Solution 2:** 0.13 g H_2PtBr_6 + 0.8 mL H_2SO_4 + 1.2 mL H_2O. Alternatively, 0.1 g $H_2PtCl_6 \cdot 6H_2O$ + 0.17 mL HBr (40%) in (2+3) H_2SO_4, make up to 2 mL. (2+3) H_2SO_4 is dilute sulfuric acid made by combining two parts (e.g. 0.8 mL) of concentrated sulfuric acid with three parts (e.g. 1.2 mL) of water. Note: Solution 2 does not keep and should be fresh when used. **Solution 3:** 2 mL H_2SO_4 + 1 mL H_2O

Test Method

Direct test: 50 µL from each of the three solutions is mixed in a spot plate. Remove 10 µL of the reagent mixture from the spot plate and add directly to sample on a glass slide. Swirl the drop two to three times with a pipette tip or glass rod, then place a coverslip on the drop. The reagent must be mixed and used within 10 minutes.

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

Crystal Morphology and Test Notes

A dark, amorphous precipitate forms quickly and turns into needles, fans, rosettes and sheaves. If the reagent is not fresh, not used within 10 minutes, or the hydromorphone concentration is low, "smudge" rosettes will form, and it may take more than an hour for typical crystals to form.

Photomicrograph of Typical Crystals

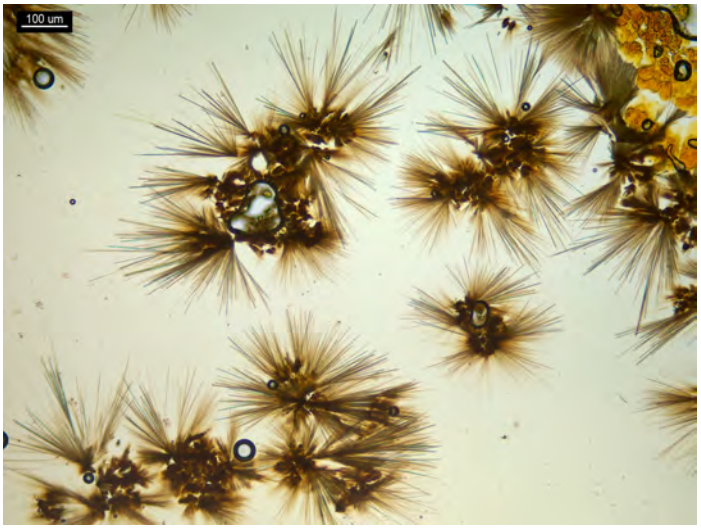


Figure 1. 1 PPP of hydromorphone and 10 µL of reagent mixture. Crystals form rosettes of needles.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on a 2 mg hydromorphone pharmaceutical tablet using 1 PPP of tablet material and 10 µL of reagent.

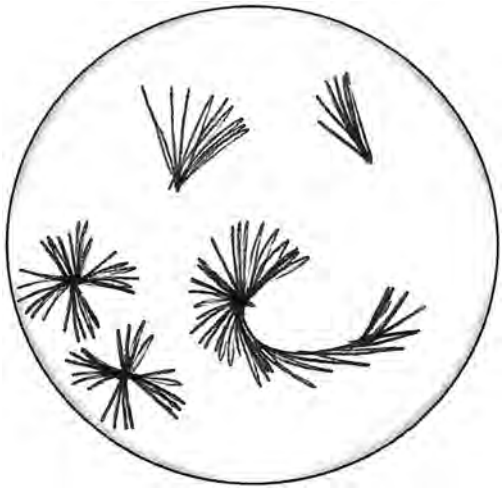
IR Spectrum

See Figure 11. Download SPC file.

PLM Optical Properties

Approximate Size Range	Rosettes: > 200 µm; individual needles: < 1 µm width, 50 µm to > 200 µm length
Color/Pleochroism	Yellow-orange. Pleochroic: golden yellow or orange (parallel) to light yellow (perpendicular)
Refractive Indices (RI)	Indeterminable

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Reagent adheres to the crystals and could not be dried. A chloroform wash was unsuccessful.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Hydromorphone: Platinum Bromide (continued)

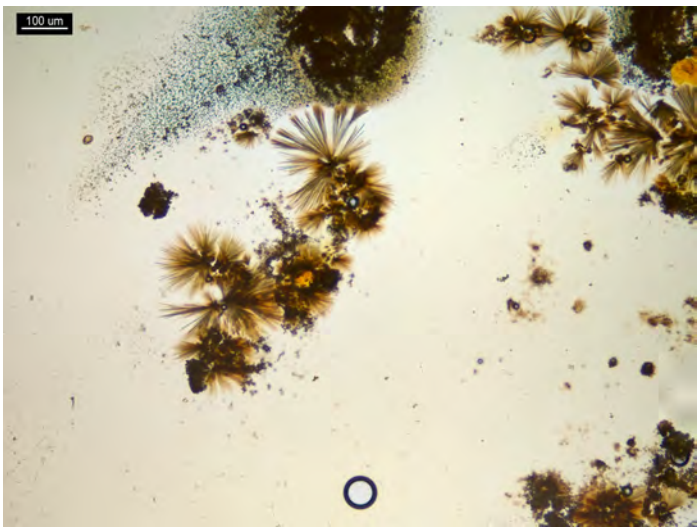

Figure 2. 1 PPP of hydromorphone and 10 µL of reagent mixture. Crystals form rosettes, sheaves, fans and needles.

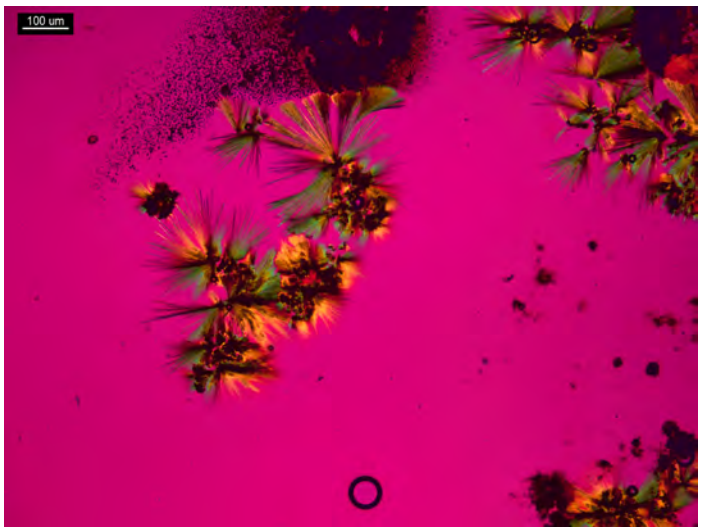

Figure 3. Same as Figure 2; crossed polars and Red I compensator.

Figure 4. 1 PPP of hydromorphone and 10 µL of reagent mixture. Pleochroism observed on thicker needles: orange (parallel) to light yellow (perpendicular); microscope polarizer is oriented East-West.

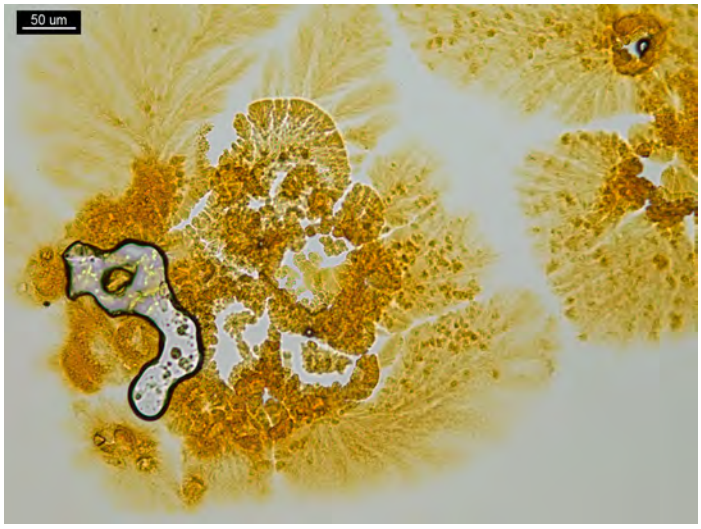

Figure 5. 1 PPP of hydromorphone and 10 µL of expired reagent mixture. The reagent must be mixed and used within 10 minutes or "smudge" rosettes form. The reagent mixture used here was 15 minutes old.

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Hydromorphone: Platinum Bromide (continued)

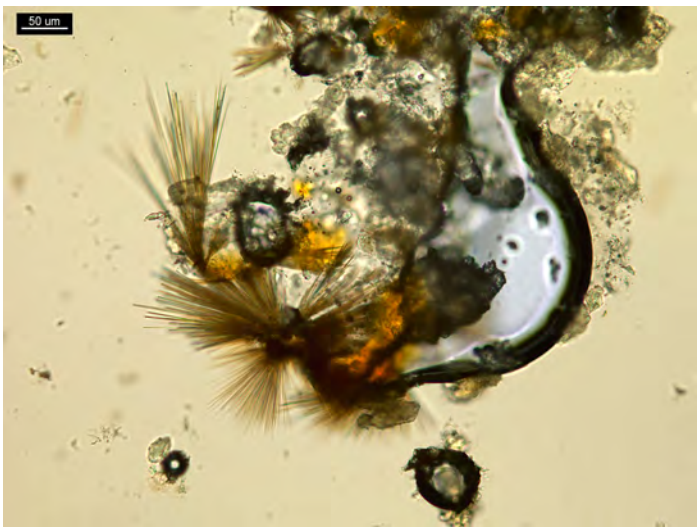

Figure 6. 10 PPP from a 2 mg hydromorphone pharmaceutical tablet and 15 µL of reagent mixture. Crystals form rosettes of needles.

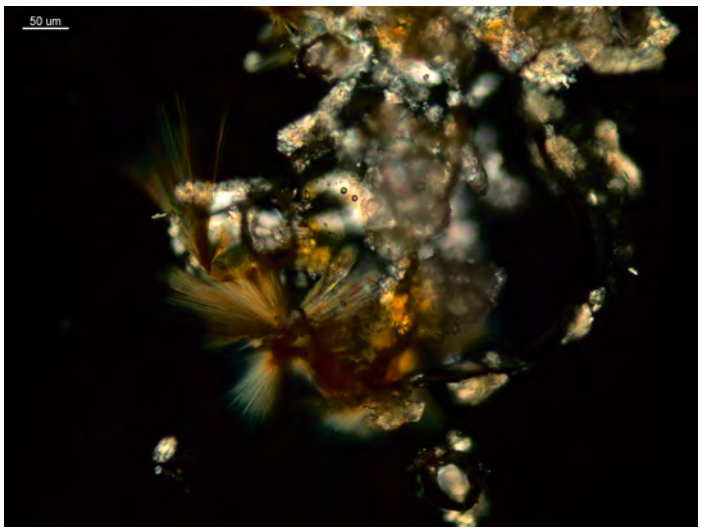

Figure 7. Same as Figure 6; crossed polars.

Figure 8. 1 PPP of hydromorphone and 10 µL of reagent mixture. Crystals form fans, rosettes and needles.

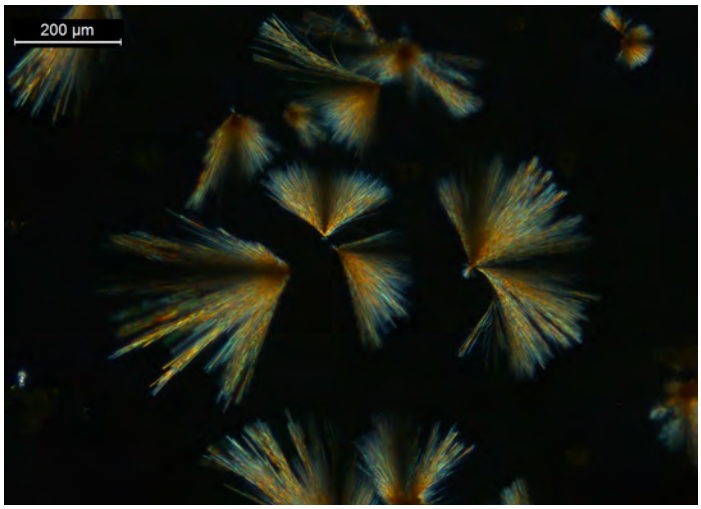

Figure 9. Same as Figure 8; crossed polars.

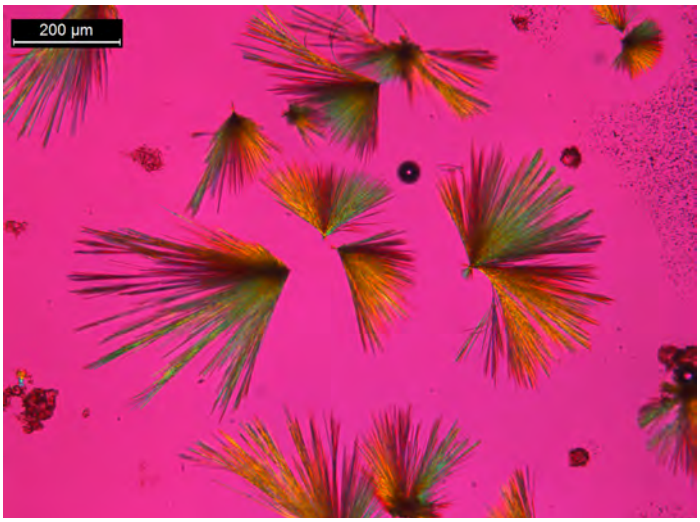

Figure 10. Same as Figure 9; crossed polars and Red I compensator.

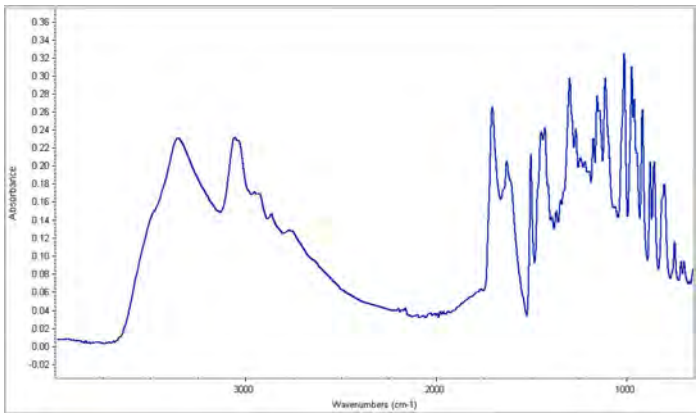

Figure 11. Infrared spectrum of hydromorphone platinum bromide precipitate. Download SPC file.

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Hydromorphone: Sodium Nitroprusside

REAGENT 2: Sodium Nitroprusside ($Na_2[Fe(CN)5NO]\cdot 2H_2O$)

1% aqueous: 0.1 g $Na_2[Fe(CN)5NO]\cdot 2H_2O$ in H_2O, make up to 10 mL. Reagent does not keep; it is pale yellow and should be used fresh before it gradually turns blue.

Test Method

Direct test: Add 5 µL of reagent directly to sample, swirl with a glass rod, toothpick or pipette tip. Wait 30–60 seconds, then draw the glass rod, toothpick or pipette tip through the drop, and crystals will form.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Less than 1 minute

Crystal Morphology and Test Notes

Rods and elongated prisms, often in rosettes and stars. Rods may have blunt ends, pointed ends or parallelogram-shaped ends. Note: This reagent, if allowed to dry with no hydromorphone present (negative control test), will form crystals with similar morphology and birefringence. However, these rods have a positive sign of elongation and should not be confused with the typical crystals formed with hydromorphone.

Photomicrograph of Typical Crystals

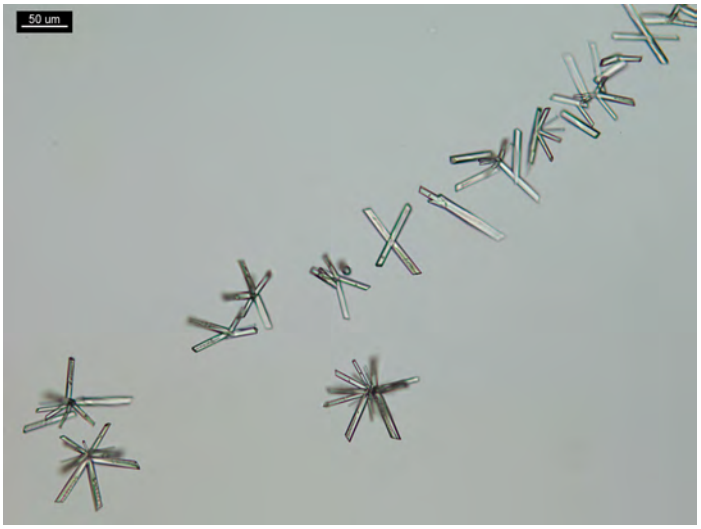


Figure 1. 1 PPP of hydromorphone and 5 µL of sodium nitroprusside reagent. Crystals form rods and elongated prisms, often in rosettes and stars.

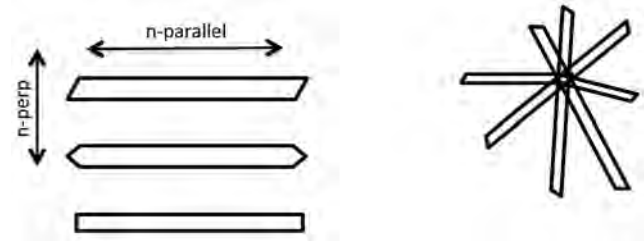
Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on a 2 mg hydromorphone pharmaceutical tablet using 3–5 PPP and 5 µL of reagent.

IR Spectrum

See Figure 8. Download SPC file.

PLM Optical Properties

Approximate Size Range	1–5 µm width, 5 to >50 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel = 1.570–1.580 n-perpendicular = 1.630– 1.660
Morphology Illustration	
How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature.
Estimated Birefringence	Moderate
Extinction	Parallel
Sign of Elongation	Negative (−)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Hydromorphone: Sodium Nitroprusside (continued)

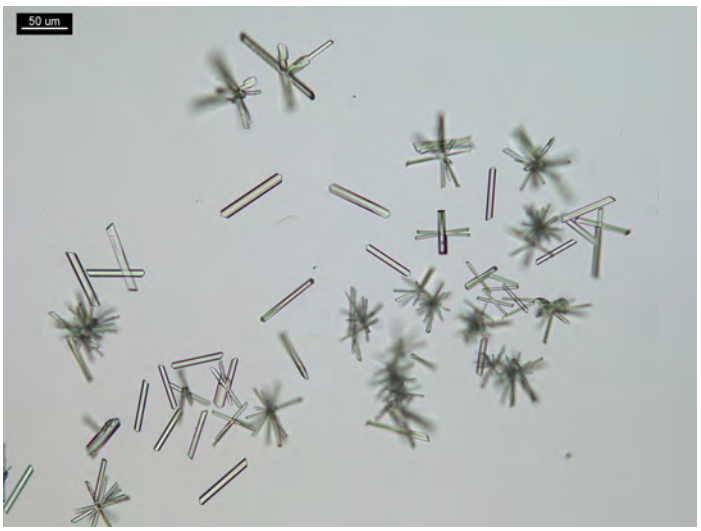

Figure 2. 1 PPP of hydromorphone and 5 µL of sodium nitroprusside reagent. Crystals form rods and elongated prisms, often in rosettes and stars.

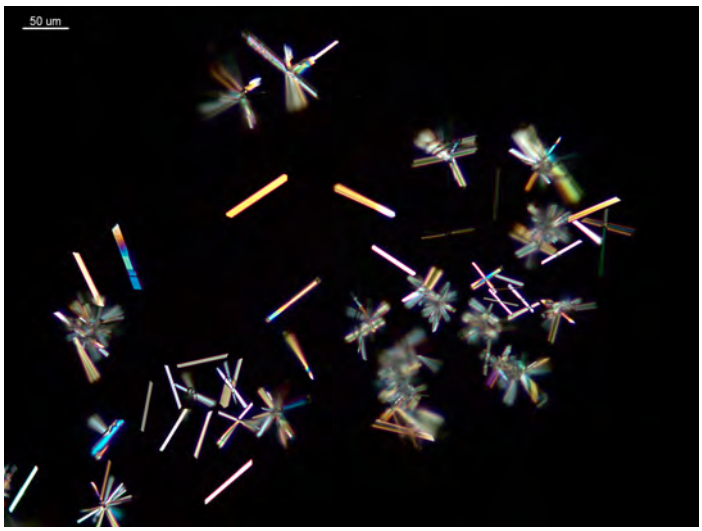

Figure 3. Same as Figure 2; crossed polars.

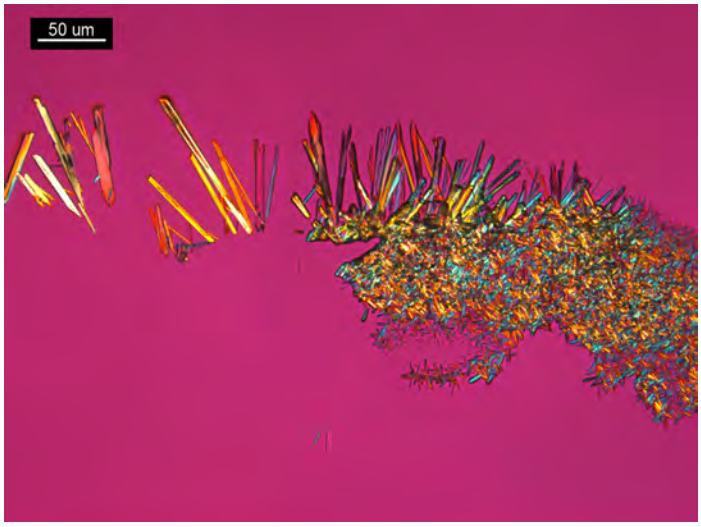

Figure 4. Sodium nitroprusside reagent dried with no hydromorphone present (negative control test). Dried reagent crystals have a positive sign of elongation; crossed polars and Red I compensator.

Figure 5. 1 PPP of hydromorphone and 5 µL of sodium nitroprusside reagent. Feather-shaped and serrated crystals formed initially near the edge of the test drop. Note: If pushed back into the center of the drop with a glass rod, toothpick or pipette tip, these crystals dissolve and recrystallize as typical rods and elongated prisms.

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Hydromorphone: Sodium Nitroprusside (continued)

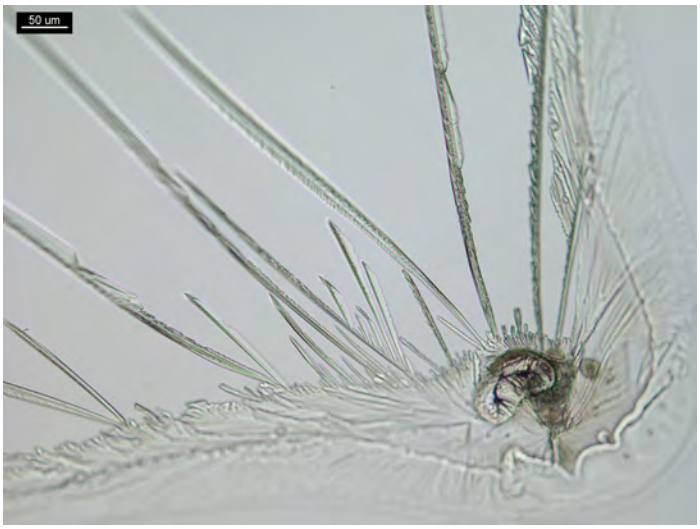

Figure 6. 1 PPP of hydromorphone and 5 µL of sodium nitroprusside reagent. Feather-shaped and serrated crystals formed initially near the edge of the test drop. Note: If pushed back into the center of the drop with a glass rod, toothpick or pipette tip, these crystals dissolve and recrystallize as typical rods and elongated prisms.

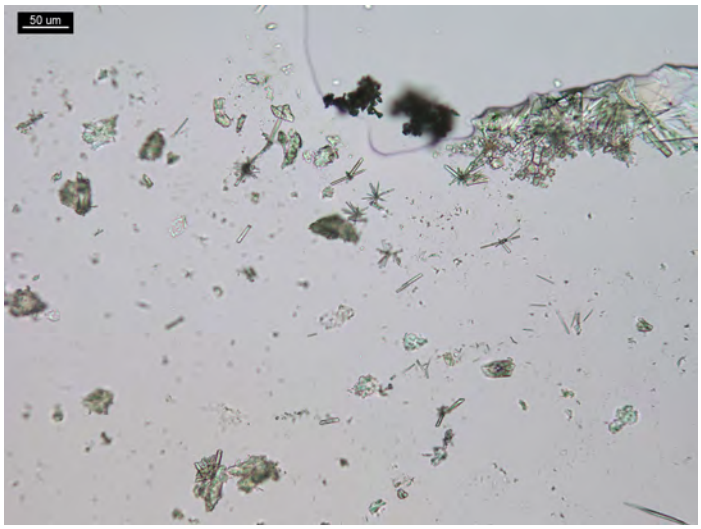

Figure 7. 3 PPP from a 2 mg hydromorphone pharmaceutical tablet and 5 µL of sodium nitroprusside reagent. Crystals form rods and elongated prisms.

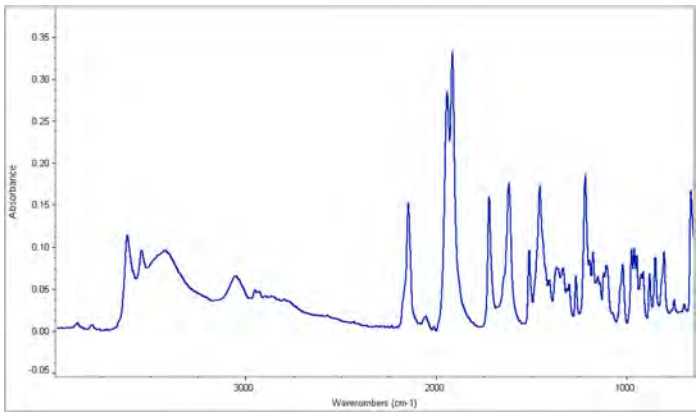

Figure 8. Infrared spectrum of hydromorphone sodium nitroprusside precipitate. Download SPC file.

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MDMA: Gold Chloride

REAGENT: Gold Chloride ($HAuCl_4$)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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: Add 5–10 µL of reagent directly to sample; no coverslip. Stir the drop with a pipette tip, glass rod or toothpick.

References

1. Ruybal, R. "Microcrystalline Test for MDMA," *Microgram*, 19:6, pp 79–80, 1986.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Oily drops form first, then X-shaped and occasional star-shaped crystals. They have a high-contrast, jagged-X internal structure surrounded by a smooth, thin crystal edge and an acute angle ≈ 19°. MDMA crystals with the $HAuCl_4$ reagent can be distinguished from *dl*-methamphetamine with $HAuCl_4$ because *dl*-methamphetamine crystals lack the high-contrast, jagged-X internal structure.

Photomicrograph of Typical Crystals

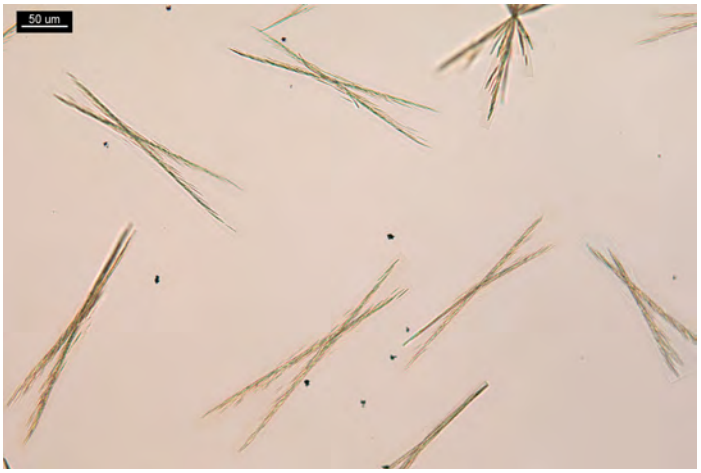


Figure 1. 1 PPP of MDMA after directly adding 5–10 µL of $HAuCl_4$ reagent. Crystals form X shapes.

Pharmaceuticals, Adulterants or Other Drug Interactions

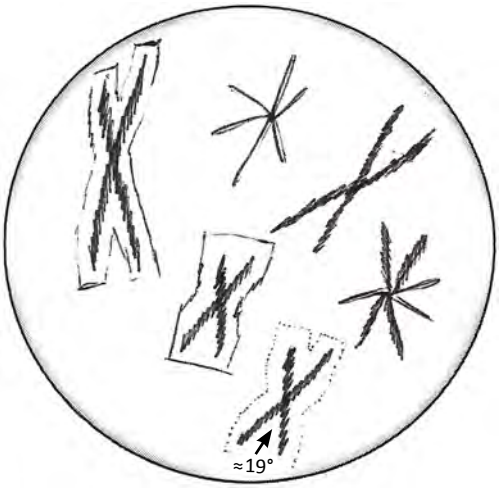
Street drug samples of MDMA may be adulterated with amphetamine, caffeine, dextromethorphan, methamphetamine, paramethoxyamphetamine or paramethoxymethamphetamine. The detectability of MDMA with selected adulterants is listed below:

- *d*-Amphetamine:MDMA – detectable at 1:5, 1:1 and 5:1
- Caffeine:MDMA – detectable at 1:5, 1:1 and 5:1
- Dextromethorphan:MDMA – detectable at 1:5, 1:1 and 5:1
- *dl*-Methamphetamine:MDMA – detectable at 1:5; detectable with distortions at 1:1; undetectable at 5:1
- Paramethoxyamphetamine:MDMA – detectable at 1:5 and 1:1; detectable with distortions at 5:1
- Paramethoxymethamphetamine:MDMA – detectable at 1:5; detectable with distortions at 1:1 and 5:1

PLM Optical Properties

Approximate Size Range	≈ 5–30 µm width, 20–500 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel slightly > 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 then washed with RI liquid.
Estimated Birefringence	Moderate–High
Extinction	Parallel to the thin crystalline edge
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 12. Download SPC file.

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MDMA: Gold Chloride (continued)

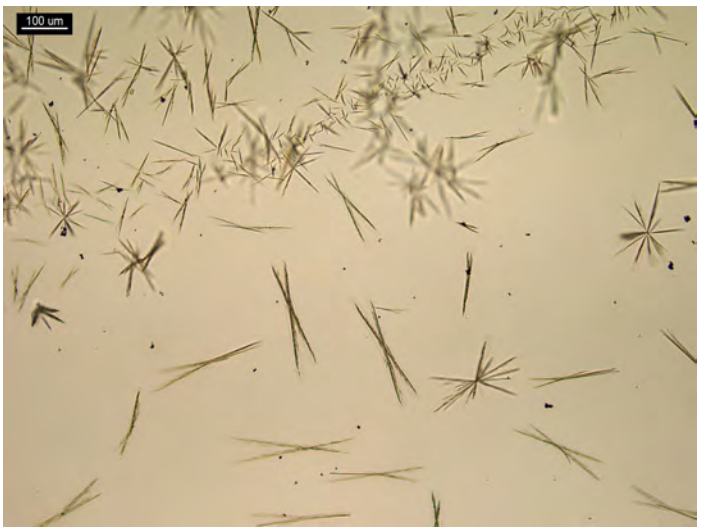

Figure 2. 1 PPP of MDMA and 5–10 µL of $HAuCl_4$ reagent. Crystals form X and star shapes.

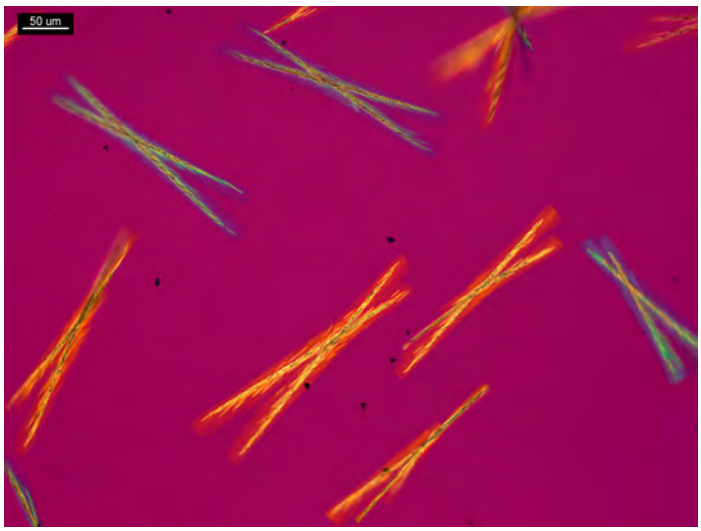

Figure 3. 1 PPP of MDMA and 5–10 µL of $HAuCl_4$ reagent. X-shaped crystals have a negative sign of elongation; crossed polars and Red I compensator.

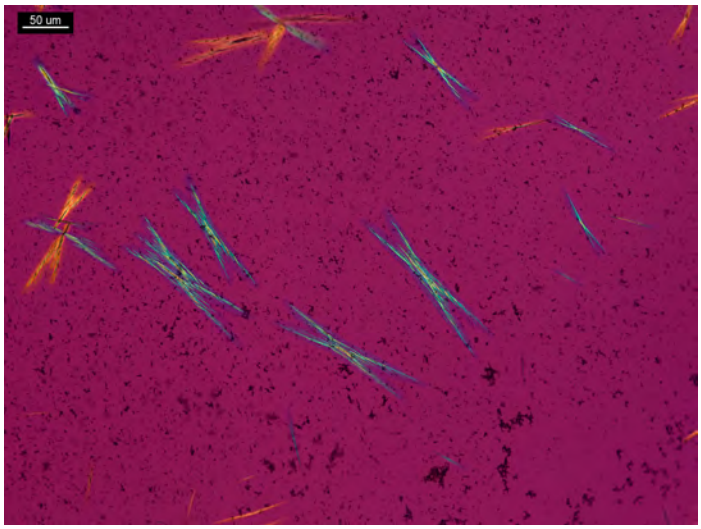

Figure 4. 1 PPP of MDMA and 5–10 µL of $HAuCl_4$ reagent. X-shaped crystals have a negative sign of elongation; crossed polars and Red I compensator.

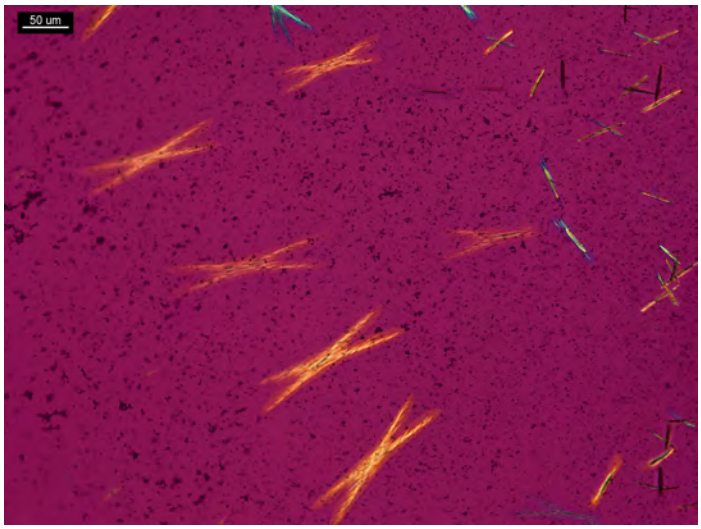

Figure 5. 1 PPP of MDMA and 5–10 µL of $HAuCl_4$ reagent. X-shaped crystals have a negative sign of elongation; crossed polars and Red I compensator.

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MDMA: Gold Chloride (continued)

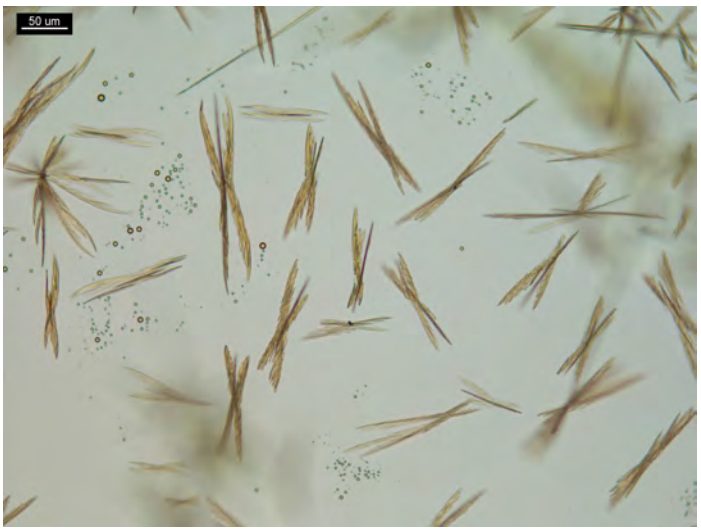

Figure 6. *d*-Amphetamine:MDMA mixture (5:1) and 5–10 µL of $HAuCl_4$ reagent. Crystals form X shapes with little or no distortion.

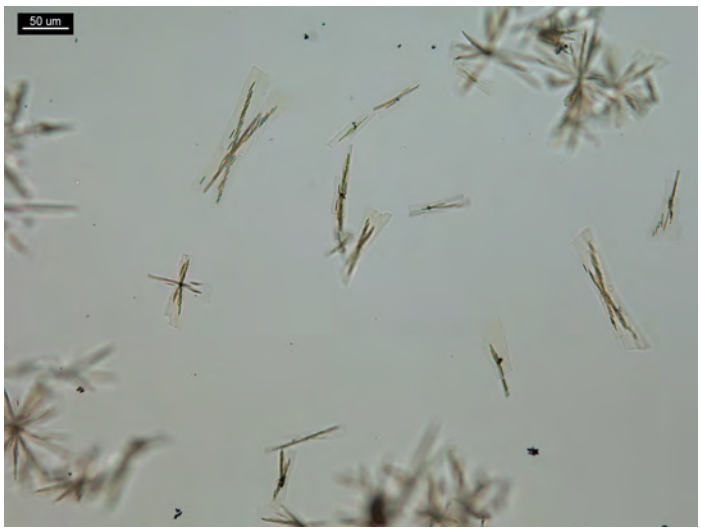

Figure 7. Dextromethorphan:MDMA mixture (5:1) and 5–10 µL of $HAuCl_4$ reagent. Crystals form X shapes with little or no distortion.

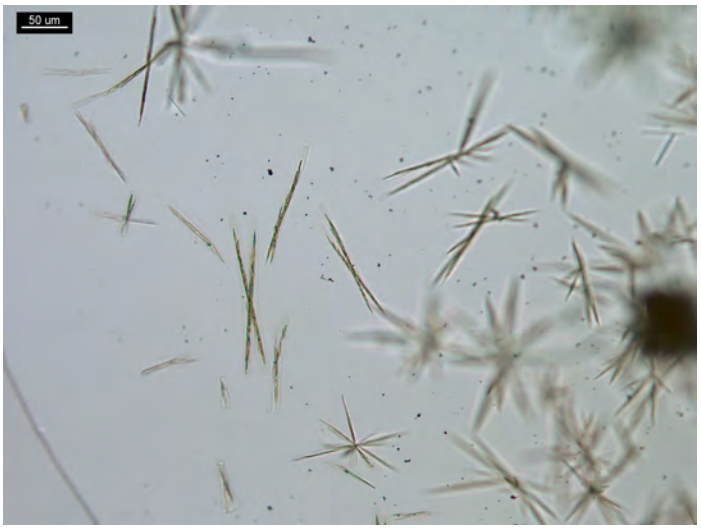

Figure 8. Caffeine:MDMA mixture (5:1) and 5–10 µL of $HAuCl_4$ reagent. Crystals form X shapes with no distortion.

Figure 9. *dl*-Methamphetamine:MDMA mixture (1:1) and 5–10 µL of $HAuCl_4$ reagent. Crystals form star shapes and a few distorted X shapes.

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MDMA: Gold Chloride (continued)

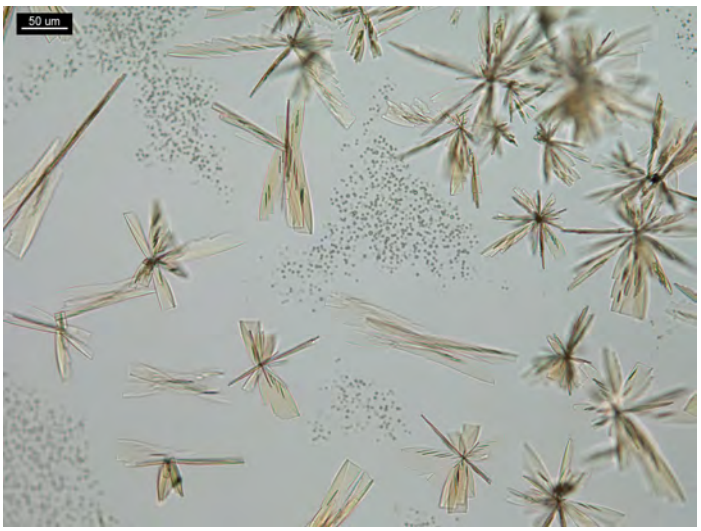

Figure 10. Paramethoxymethamphetamine:MDMA mixture (1:1) and 5–10 µL of $HAuCl_4$ and (1+2) H_3PO_4 reagent. Crystals are distorted, do not appear X-shaped, but are shaped like tablets and clusters.

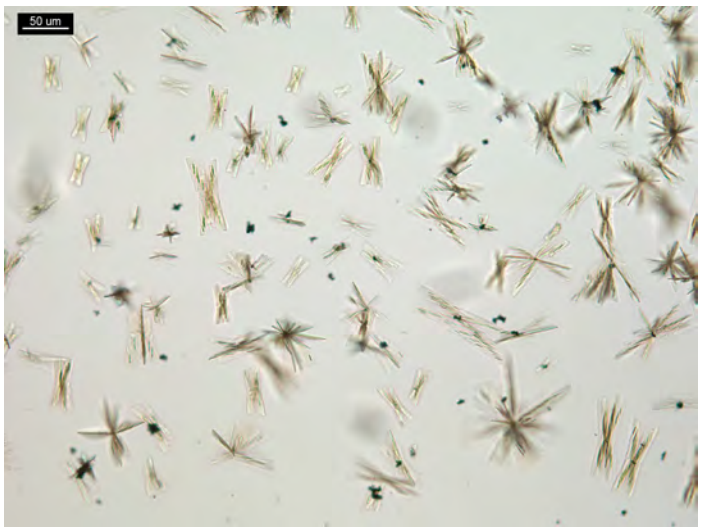

Figure 11. Paramethoxyamphetamine:MDMA (5:1) and 5–10 µL of $HAuCl_4$ and (1+2) H_3PO_4 reagent. X-shaped crystals, tablets and clusters. The X-shaped crystals are shorter and wider than MDMA-gold chloride crystals.

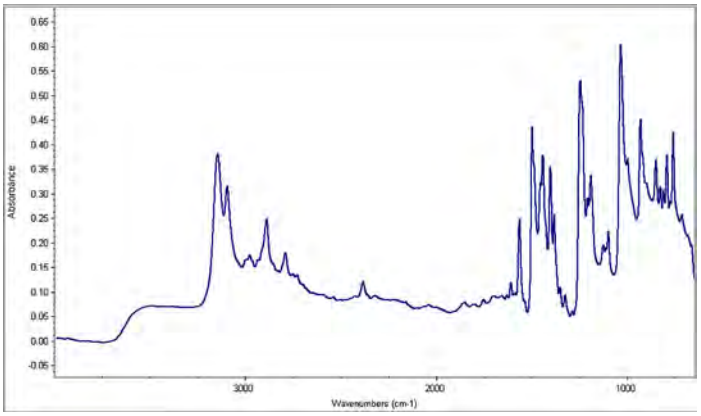

Figure 12. Infrared spectrum of MDMA gold chloride precipitate. Download SPC file.

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Methadone: Mercuric Chloride

REAGENT 1: Mercuric Chloride ($HgCl_2$)

5% aqueous: 1 g $HgCl_2$ in H_2O, make up to 20 mL

Test Method

Direct test: Place sample on a glass slide, add 3 µL of 2 N HOAc and 5 µL of reagent, mix with a pipette tip, glass rod or toothpick.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP (up to 3 PPP for pharmaceuticals)

Time Required for Crystal Formation

≈ 1–6 minutes (pharmaceutical tablets ≈ 10 minutes)

Crystal Morphology and Test Notes

Rosettes, clusters, burrs, fans, sheaves, and tufts of needles and rods, sometimes branching and dendritic. Wrapped candy-shaped crystals are also visible (Figure 4).

Photomicrograph of Typical Crystals

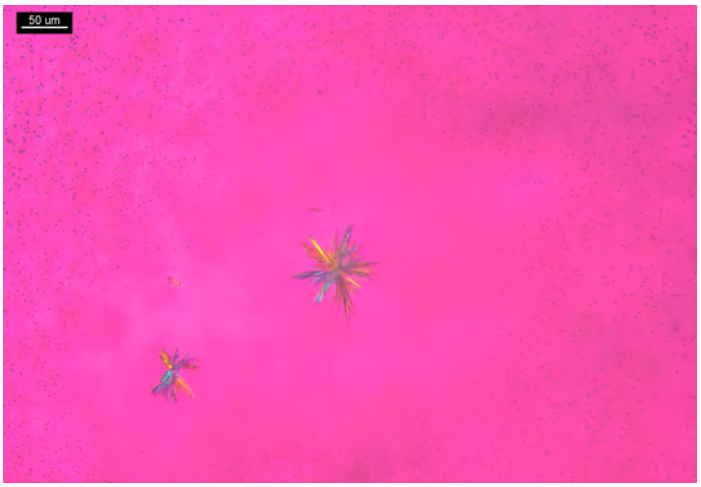


Figure 1. 1 PPP of methadone and 3 µL 2 N HOAc and 5 µL of $HgCl_2$ reagent. Crystals form rosettes and clusters in a hanging drop (after ≈ 4 minutes); crossed polars and Red I compensator.

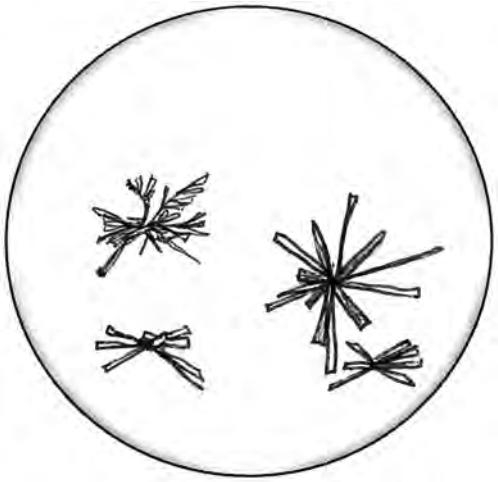
Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 mg and 10 mg methadone tablets, which required up to 3 PPP of tablet material and up to 10 minutes for typical crystal formation. This test was also successful using 10 µL of methadone hydrochloride oral solution (5 mg/5 mL) directly; no extraction was necessary, but the 2 N HOAc was omitted because it appeared to hinder crystal growth. If an extraction is required: 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/methadone (bottom) layer into a clean microcentrifuge tube. Adjust to pH 6 with 10% HCl and shake. Use a micropipette to decant 10 µL aliquots onto a glass slide or coverslip, allowing each drop to evaporate before adding another drop, then proceed with test method.

PLM Optical Properties

Approximate Size Range	10 to > 200 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n-parallel ≈ 1.658 n-perpendicular 1.630–1.660

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then dried at room temperature.
Estimated Birefringence	Moderate
Extinction	Parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 9. Download SPC file.

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Methadone: Mercuric Chloride (continued)

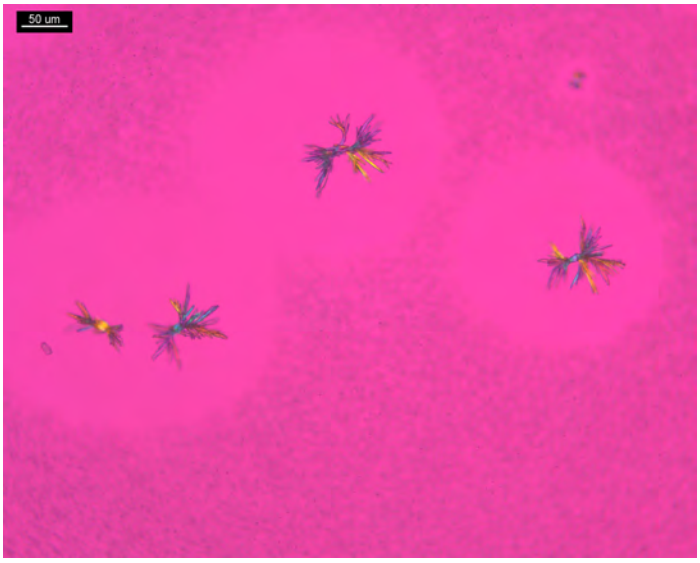

Figure 2. 1 PPP of methadone and 3 µL 2 N HOAc and 5 µL of $HgCl_2$ reagent (after ≈ 3 minutes). Crystals form fans and sheaves; crossed polars and Red I compensator.

Figure 3. 1 PPP of methadone and 3 µL 2 N HOAc and 5 µL of $HgCl_2$ reagent (after ≈ 6 minutes). Crystals form fans and sheaves and dendrites; crossed polars and Red I compensator.

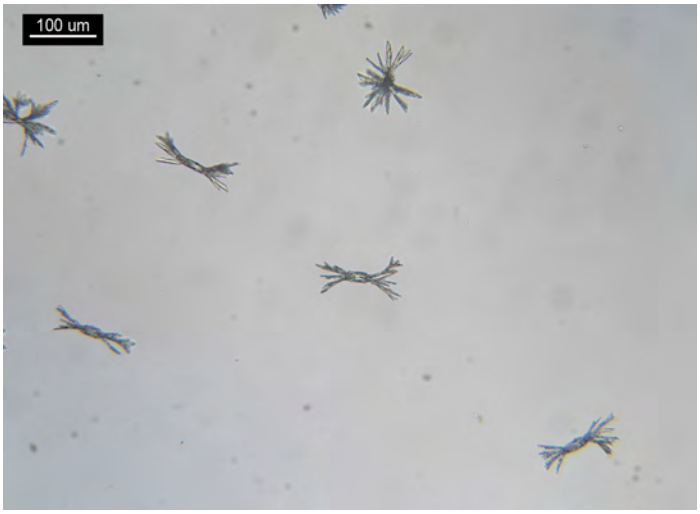

Figure 4. 1 PPP of methadone and 3 µL 2 N HOAc and 5 µL of $HgCl_2$ reagent; no coverslip. Crystals form rosettes and sheaves resembling wrapped candy.

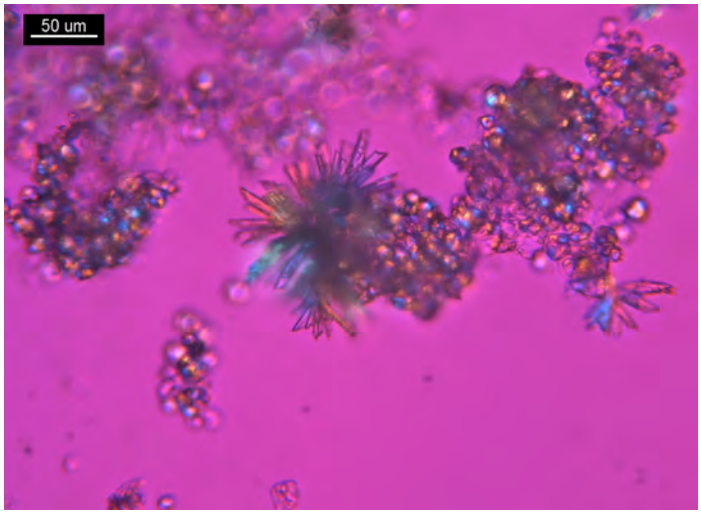

Figure 5. 3 PPP from a 5 mg methadone tablet and 3 µL 2 N HOAc and 5 µL of $HgCl_2$ reagent. Crystals form rosettes; crossed polars and Red I compensator.

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Methadone: Mercuric Chloride (continued)

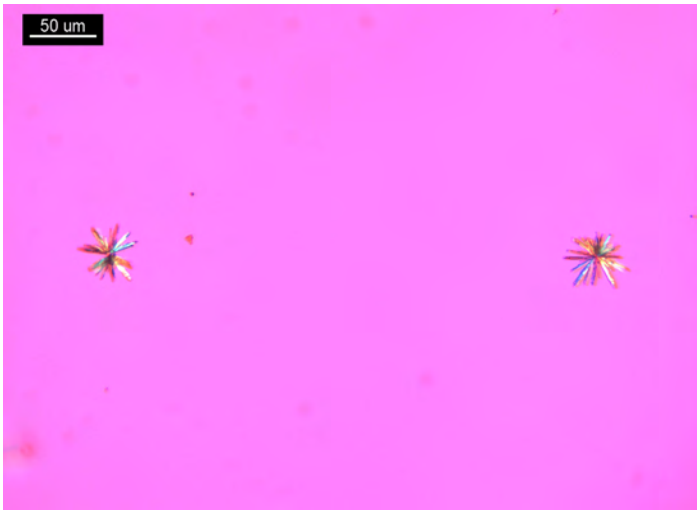

Figure 6. 10 µL from a methadone hydrochloride oral solution (5 mg/5 mL) and 5 µL of $HgCl_2$ reagent (after ≈ 3 minutes). No extraction was necessary. Crystals form rosettes; crossed polars and Red I compensator.

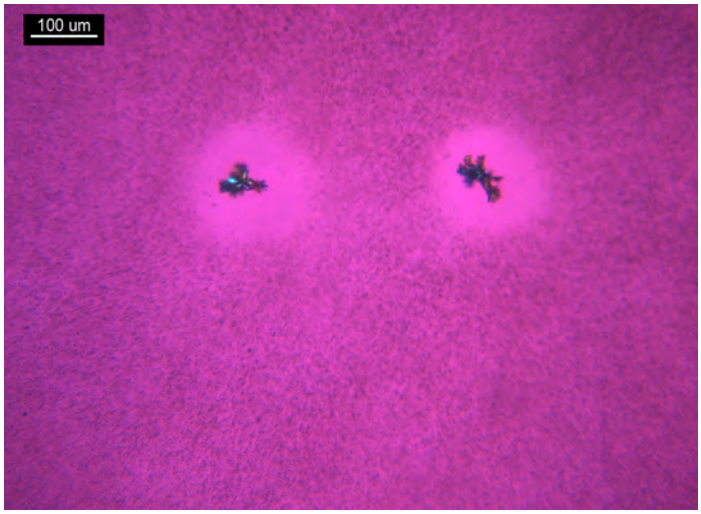

Figure 7. 50 µL after extraction procedure from a 5 mg/5 mL methadone hydrochloride oral solution and 5 µL of $HgCl_2$ reagent (after ≈ 2 minutes). Crystals form sheaves; crossed polars and Red I compensator.

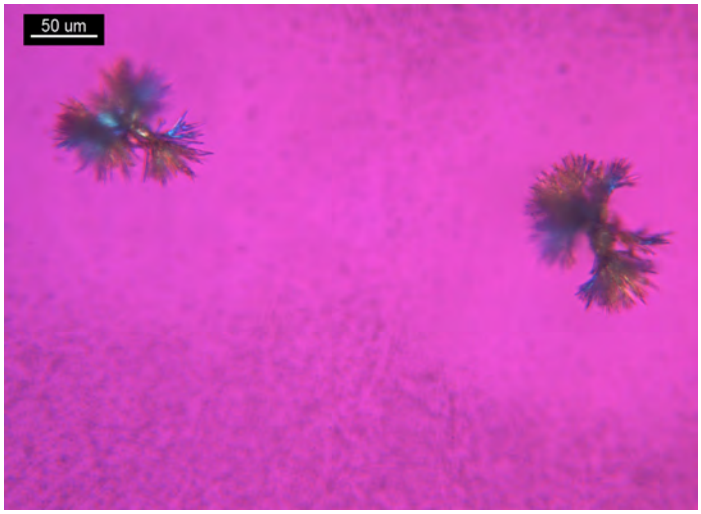

Figure 8. 50 µL after extraction procedure from a 5 mg/5 mL methadone hydrochloride oral solution and 5 µL of $HgCl_2$ reagent (after ≈ 4 minutes). Crystals form sheaves and dendrites; crossed polars and Red I compensator.

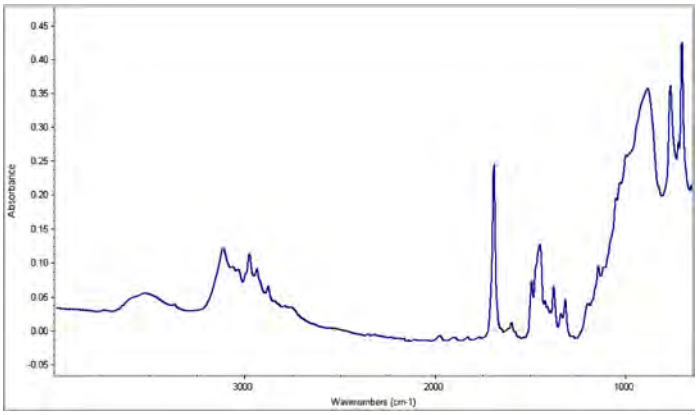

Figure 9. Infrared spectrum of methadone mercuric chloride precipitate. Download SPC file.

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Methadone: Mercuric Bromide

REAGENT 2: Mercuric Bromide ($HgBr_2$)

5 g $HgBr_2$ in 22 mL concentrated HCl. Add H_2O to make up to 100 mL.

Test Method

Direct test: Place sample on a glass slide and add 3 µL of 1% HCl. Place a 3 µL drop of reagent on a coverslip. Invert the coverslip and place it directly onto the sample. Oral solutions may require up to 5 µl of reagent.

References

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

Limit of Detection

1 PPP or less

Time Required for Crystal Formation

< 1 minute

Crystal Morphology and Test Notes

Rosettes, stars, sheaves, dendrites and clusters of needles. Some are feathered or jagged blades and often resemble an X shape.

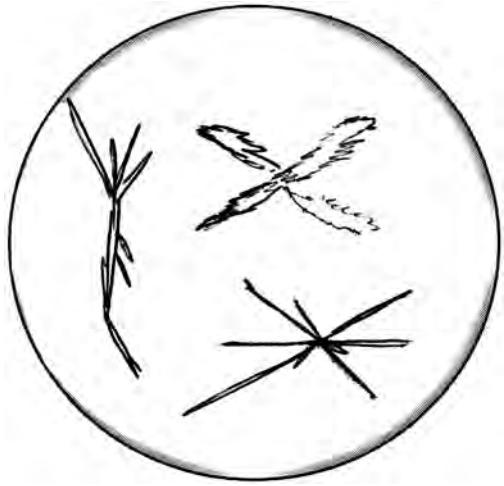
Photomicrograph of Typical Crystals

Figure 1. 1 PPP of methadone and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent (after ≈ 4 minutes). Crystals form rosettes, stars and clusters of needles; crossed polars and Red I compensator.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 mg and 10 mg methadone tablets using a sample size as small as 1 PPP. This test was also successful using 10 µL of methadone hydrochloride oral solution (5 mg/5 mL) directly; no extraction was necessary. If an extraction is required: 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/methadone (bottom) layer into a clean microcentrifuge tube. Adjust to pH 6 with 10% HCl and shake. Use a micropipette to decant 10 µL aliquots onto a glass slide, allowing each drop to evaporate before adding another drop, then proceed with test method.

PLM Optical Properties

Approximate Size Range	50 to > 100 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	$n_1 \approx 1.640$ $n_2 \approx 1.690$
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then washed with absolute ethanol using a tungsten needle and dried at room temperature.
Estimated Birefringence	Moderate–High
Extinction	Needles: parallel Jagged blades: oblique
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 14. Download SPC file.

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Methadone: Mercuric Bromide (continued)

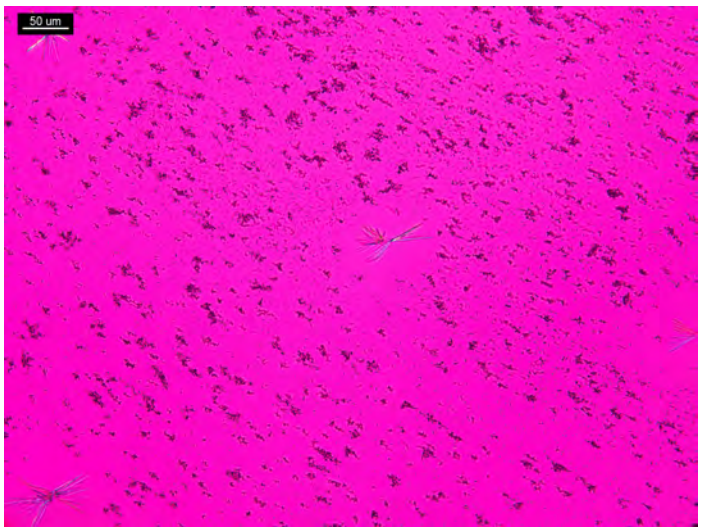

Figure 2. 1 PPP of methadone and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent (after ≈ 1 minute). Crystals form sheaves; crossed polars and Red I compensator.

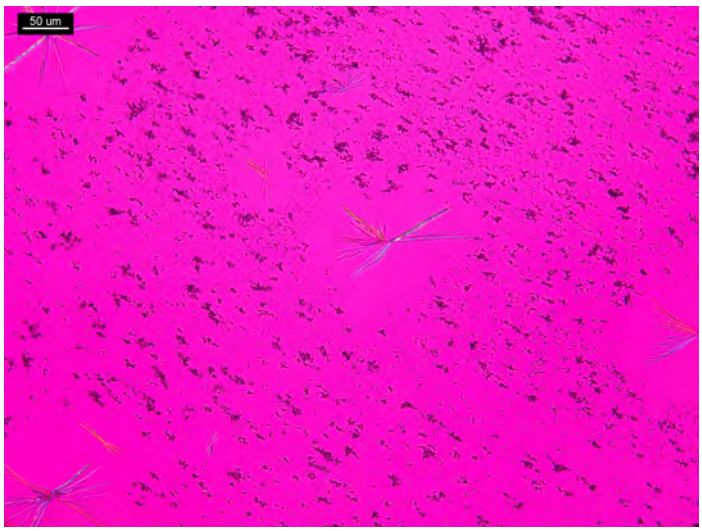

Figure 3. 1 PPP of methadone and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent (after ≈ 2 minutes). Crystals form sheaves; crossed polars and Red I compensator.

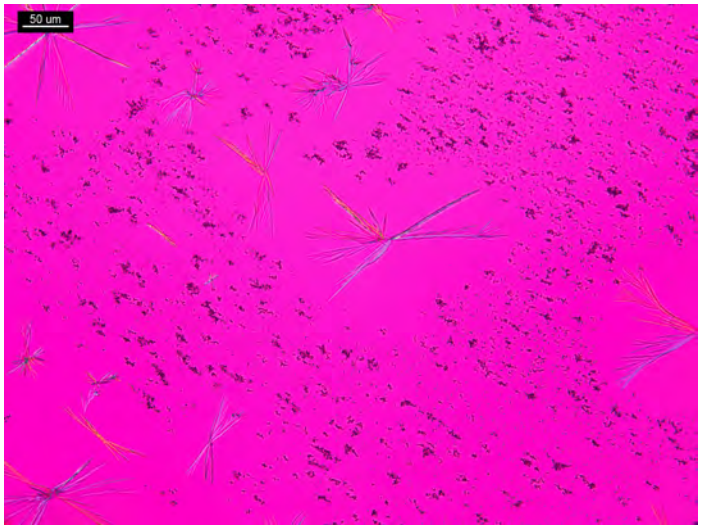

Figure 4. 1 PPP of methadone and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent (after ≈ 3 minutes). Crystals form sheaves and dendrites; crossed polars and Red I compensator.

Figure 5. 1 PPP of methadone and 3 µL 1% of HCl and 3 µL of $HgBr_2$ reagent (after ≈ 5 minutes). Crystals form sheaves and dendrites; crossed polars and Red I compensator.

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Methadone: Mercuric Bromide (continued)

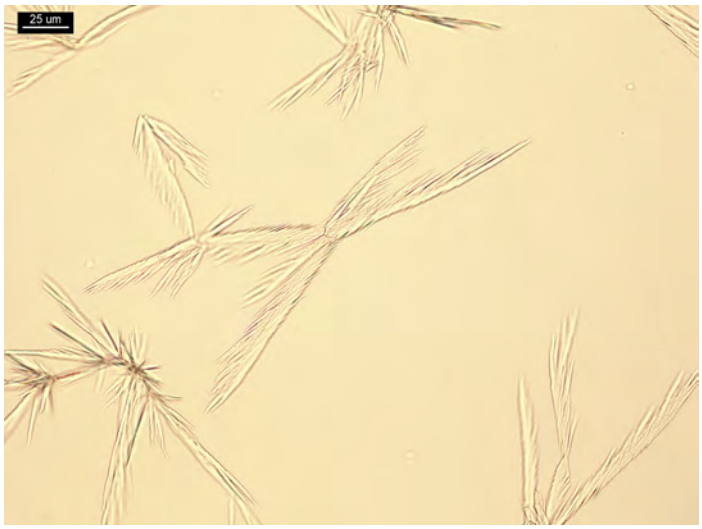

Figure 6. 1 PPP of methadone and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent. Crystals form feathery X shapes.

Figure 7. Same as Figure 6; crossed polars.

Figure 8. Same as Figure 6; crossed polars and Red I compensator.

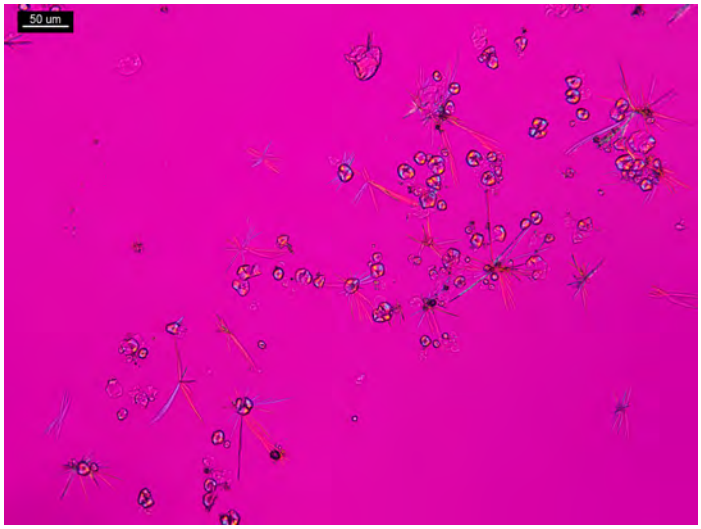

Figure 9. 1 PPP from a 5 mg methadone pharmaceutical tablet and 3 µL of 1% HCl and 3 µL of $HgBr_2$ reagent. Crystals form stars and clusters of needles; crossed polars and Red I compensator.

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Methadone: Mercuric Bromide (continued)

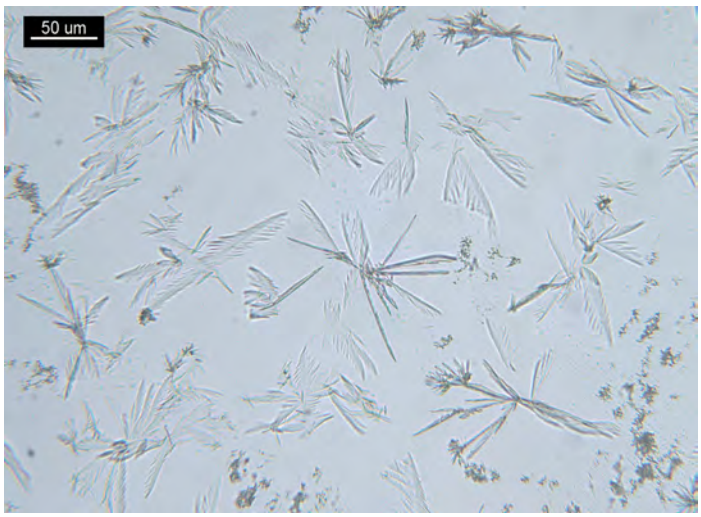

Figure 10. 50 µL of extract (after extraction procedure) from a 5 mg/5 mL methadone hydrochloride oral solution and 5 µL of $HgBr_2$. Crystals form feathers and X shapes.

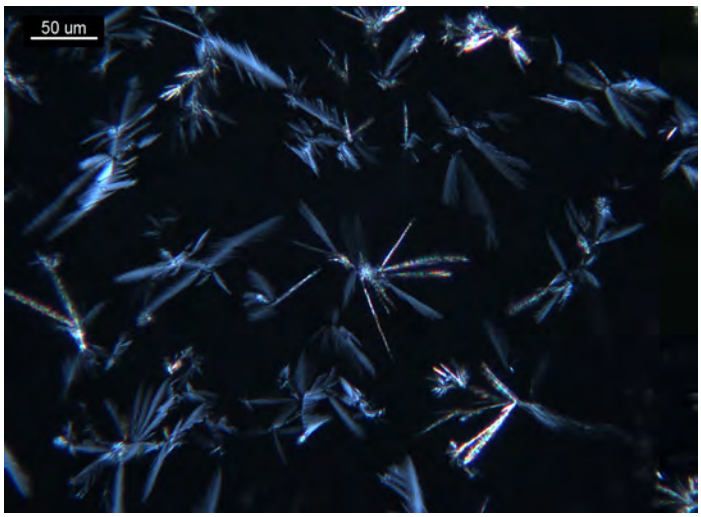

Figure 11. Same as Figure 10; crossed polars.

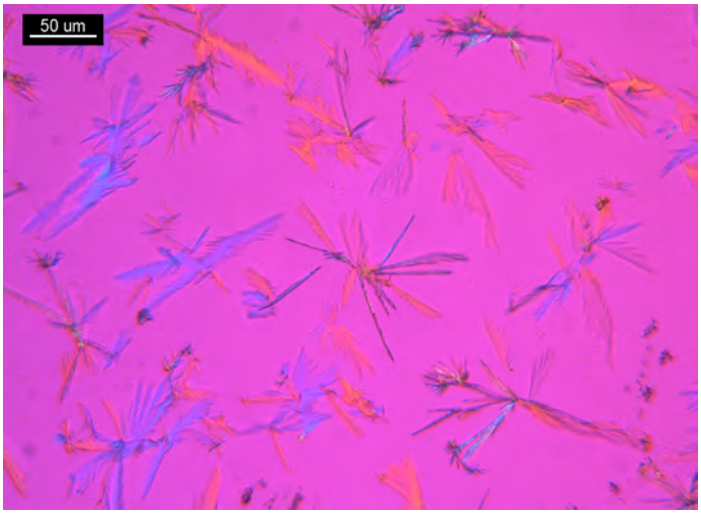

Figure 12. Same as Figure 10; crossed polars and Red I compensator.

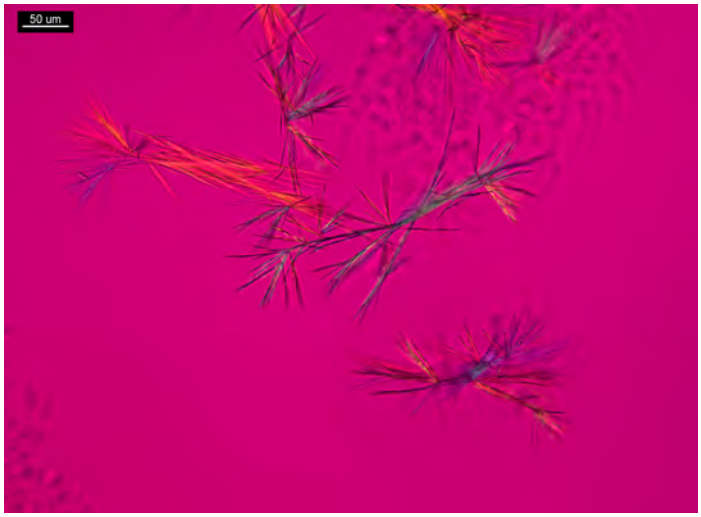

Figure 13. 10 µL from a methadone hydrochloride oral solution (5 mg/5 mL) and 3 µL of 1% HCl and 5 µL of $HgBr_2$ reagent. No extraction was necessary. Crystals form rosettes of needles and stars; crossed polars and Red I compensator.

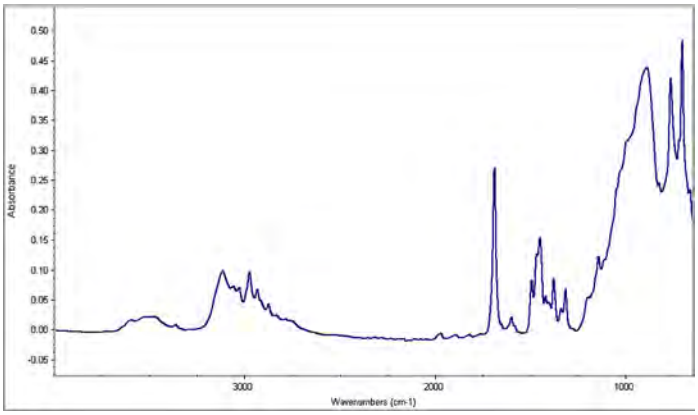

Figure 14. Infrared spectrum of methadone mercuric bromide precipitate. Download SPC file.

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d-Methamphetamine: Gold Chloride

REAGENT 1: Gold Chloride ($HAuCl_4$)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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

There are two test methods, volatility and direct; both produce the same crystals. **Direct test:** Add 5–10 µL of reagent directly to sample; gentle stirring is optional. Or, dissolve sample in 2 µL concentrated H_3PO_4 or (1+2) H_3PO_4, then add 5 µL of reagent and gently mix drop with pipette tip, glass rod or toothpick to induce crystallization; typical crystals may not form without performing this step. **Volatility test:** With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring. After 5 minutes, or longer if oily drops do not form at the edge of the hanging drop, remove coverslip and place faceup to expose hanging drop to air.

References

1. ASTM Designation E1969-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.
3. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Direct: Immediate, if the reagent is added directly to the sample, or < 5 minutes if the sample is first dissolved in concentrated H_3PO_4 or (1+2) H_3PO_4. **Volatility:** < 5 minutes.

Crystal Morphology and Test Notes

Clothespins, forked rods, blades, swallow tails, wheat and tufts. Volatility test also produces dendritic and branched clusters.

Photomicrograph of Typical Crystals

Figure 1. Direct test: 1 PPP of *d*-methamphetamine with 5-10 µL of $HAuCl_4$ reagent. Clothespins, forked rods and swallow tails form instantly.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on street drug samples of *d*-methamphetamine, including those adulterated with caffeine, dimethylsulfone or ephedrine. These common adulterants with *d*-methamphetamine in ratios of 1:1 and 5:1 (adulterant: methamphetamine) had no apparent effect on this test.

PLM Optical Properties

Approximate Size Range	10 µm width, 100 µm length; length can be > 500 µm
Color/Pleochroism	Yellow. Pleochroic: colorless (parallel) to pale yellow (perpendicular); may not be apparent on thin crystals.
Refractive Indices (RI)	n-parallel ≈ 1.560 n-perpendicular > 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 RI liquid.
Estimated Birefringence	High
Extinction	Parallel on individual rods
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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d-Methamphetamine: Gold Chloride (continued)

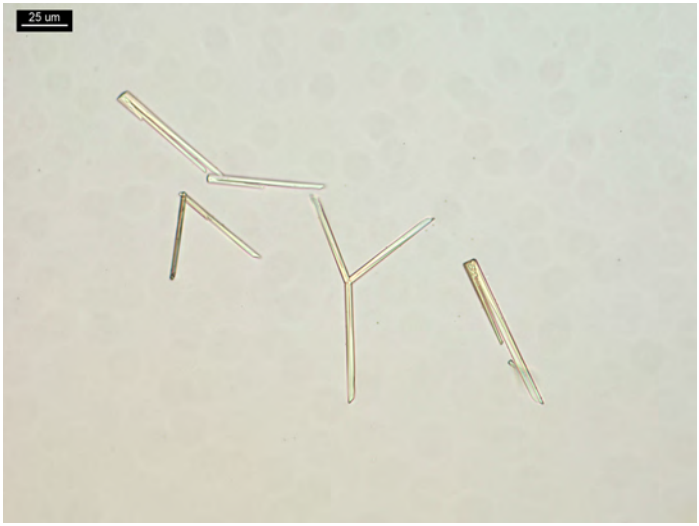

Figure 2. Direct test: 1 PPP of *d*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent. Clothespins, forked rods and swallow tails form instantly.

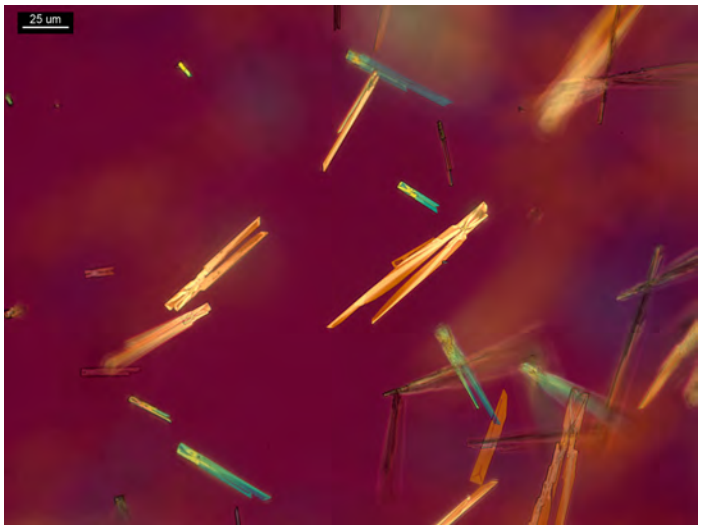

Figure 3. Direct test: 1 PPP of *d*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent; crossed polars and Red I compensator.

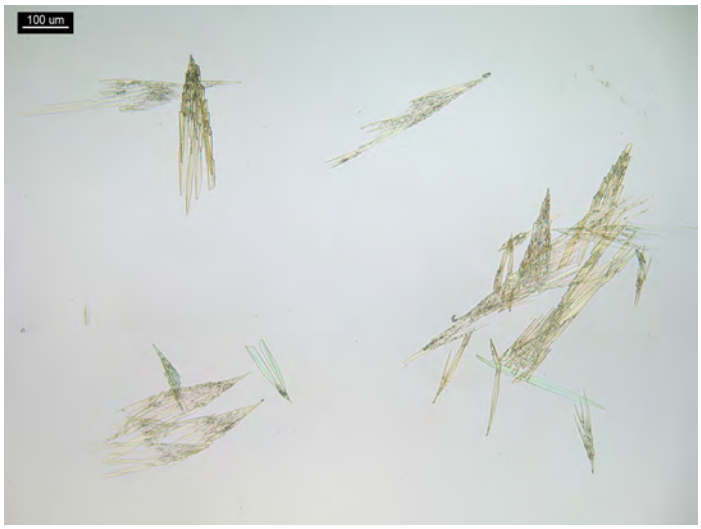

Figure 4. Direct test: 1 PPP of *d*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent. Crystals are wheat- and swallow-tail shaped. Colorless to yellow pleochorism is apparent on the two crystals in the upper left corner.

Figure 5. Same as Figure 4; crossed polars.

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d-Methamphetamine: Gold Chloride (continued)

Figure 6. Same as Figure 4; crossed polars and Red I compensator.

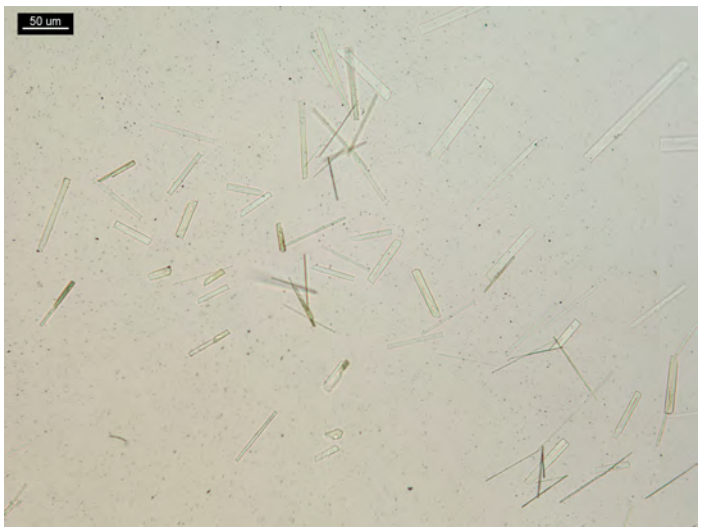

Figure 7. Direct test: 1 PPP of *d*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent. Crystals form rods.

Figure 8. Direct test: 1 PPP of *d*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent. Large swallow tail- or clothespin-shaped crystals are surrounded by short rods.

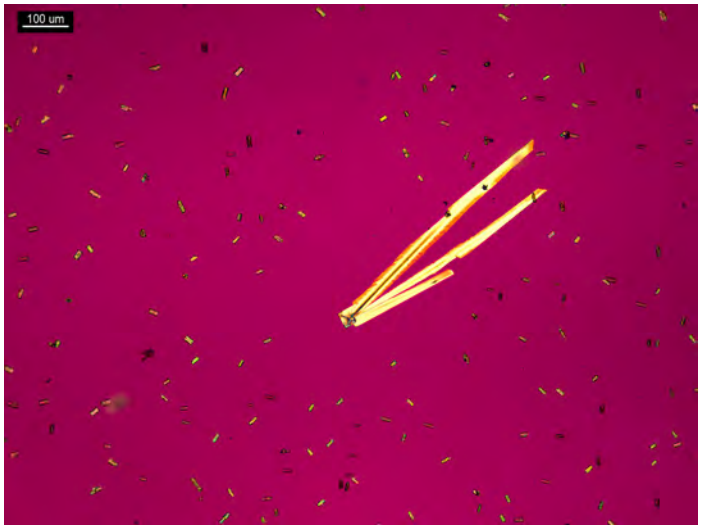

Figure 9. Same as Figure 8; crossed polars and Red I compensator.

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d-Methamphetamine: Gold Chloride (continued)

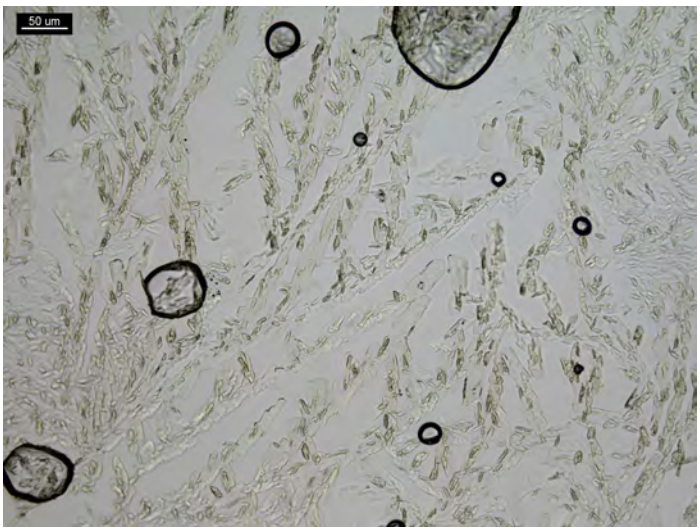

Figure 10. Volatility test: 1 PPP of *d*-methamphetamine and 5 µL of $HAuCl_4$ reagent. Crystals form dendritic and branched clusters in addition to clothespins and rods.

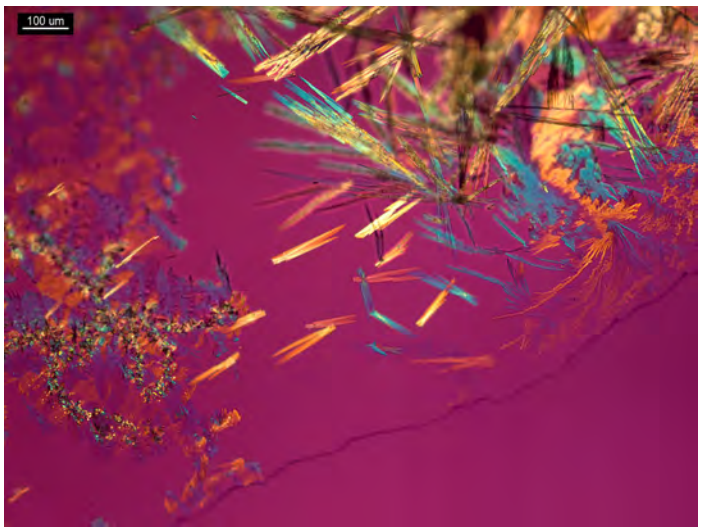

Figure 11. Direct test: Dimethylsulfone and *d*-methamphetamine (5:1) and 5–10 µL of $HAuCl_4$ reagent. Crystals form clothespins; crossed polars and Red I compensator.

Figure 12. Direct test: 1 PPP from a street drug sample of ice (a pure form of methamphetamine) and 5–10 µL of $HAuCl_4$ reagent. Clothespins form instantly; crossed polars and Red I compensator.

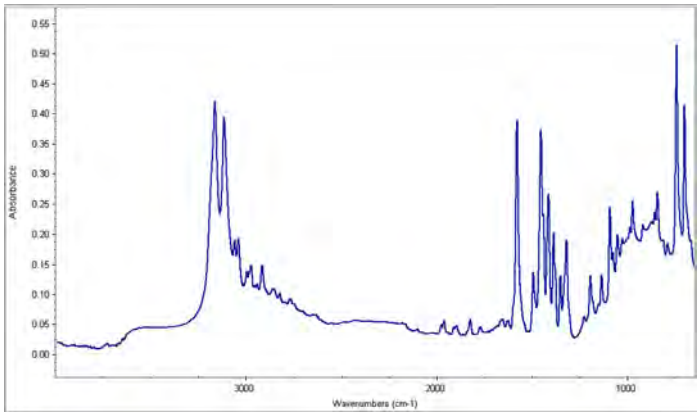

Figure 13. Infrared spectrum of *d*-methamphetamine gold chloride precipitate. Download SPC file.

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d-Methamphetamine: Platinum Chloride

REAGENT 2: Platinum Chloride (H_2PtCl_6)

There are two reagents; both produce the same crystals: **1 g $H_2PtCl_6 \cdot 6H_2O$ in (1+3) H_3PO_4,** make up to 20 mL. (1+3) H_3PO_4 is dilute phosphoric acid made by combining one part (e.g. 5 mL) of concentrated phosphoric acid with three parts (e.g. 15 mL) of water (direct or volatility test methods). **5% aqueous:** 1 g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 20 mL (direct test method only)

Test Method

There are two test methods: direct and volatility; each produce different crystals. **Direct test:** Dissolve sample in 5 µL concentrated H_3PO_4, then add 5 µL of reagent to the edge of the acid drop; crystals form instantly. **Volatility test:** With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL H_2PtCl_6 and (1+3) H_3PO_4 drop on a coverslip, invert the coverslip and cover the glass ring.

References

1. ASTM Designation E1969-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.
3. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Direct: Immediate
Volatility: < 5 minutes

Crystal Morphology and Test Notes

d-Methamphetamine crystals are similar to *dl*-methamphetamine crystals with the same platinum chloride reagent. **Direct:** Dendrites, X-shaped crystals, pinwheel and bushy rosettes. Six-sided prisms may form over time. **Volatility:** Triangular tablets, six-sided prisms, and irregular and textured plates.

Photomicrograph of Typical Crystals

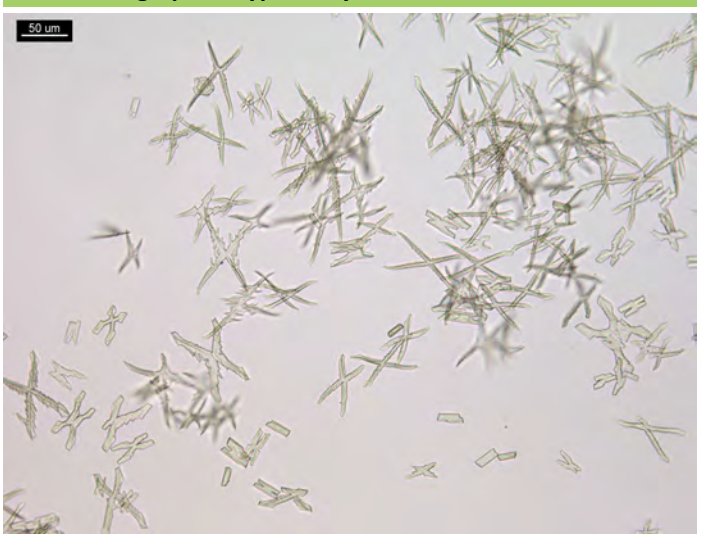


Figure 1. Direct test: 1 PPP of *d*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Dendrites and X-shaped crystals form instantly.

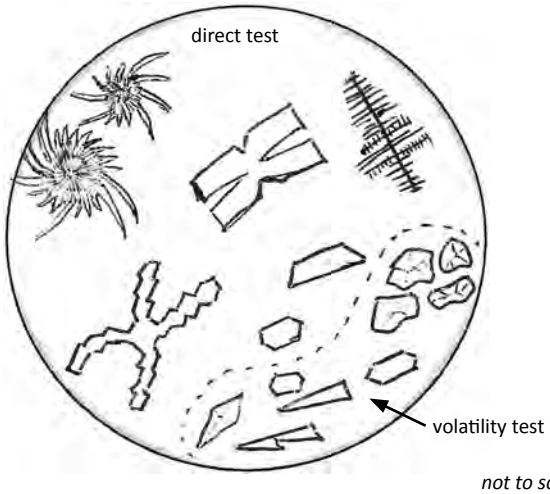
Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on street drug samples of *d*-methamphetamine, including those adulterated with caffeine, dimethylsulfone or ephedrine. These common adulterants with *d*-methamphetamine in ratios of 1:1 and 5:1 (adulterant:methamphetamine) had no apparent effect on this test.

PLM Optical Properties

Approximate Size Range	5 µm width, 100 µm length; length can be > 300 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	All RIs > 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 RI liquid.
Estimated Birefringence	Moderate
Extinction	Prisms: parallel and symmetrical Pinwheel rosettes: undulose Some X-shaped crystals showed dispersed extinction (blue-gray to pale yellow)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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d-Methamphetamine: Platinum Chloride (continued)

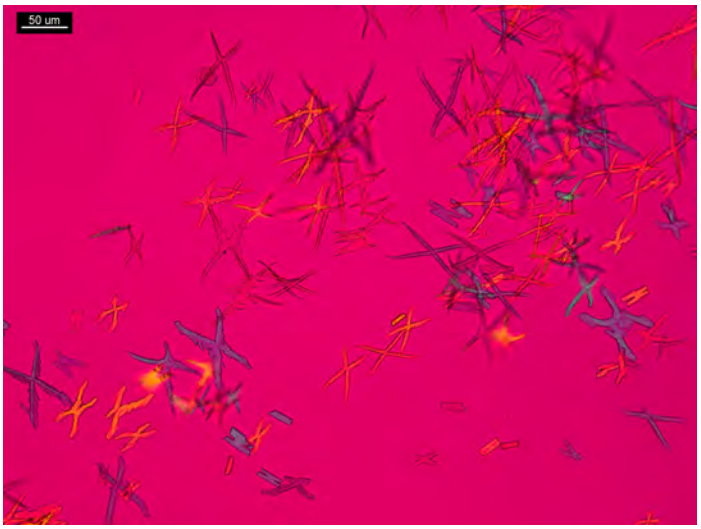

Figure 2. Direct test: 1 PPP of of *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Crystals form X-shaped and prisms; crossed polars and Red I compensator.

Figure 3. 1 PPP of of *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Crystals form dendrites and X-shaped.

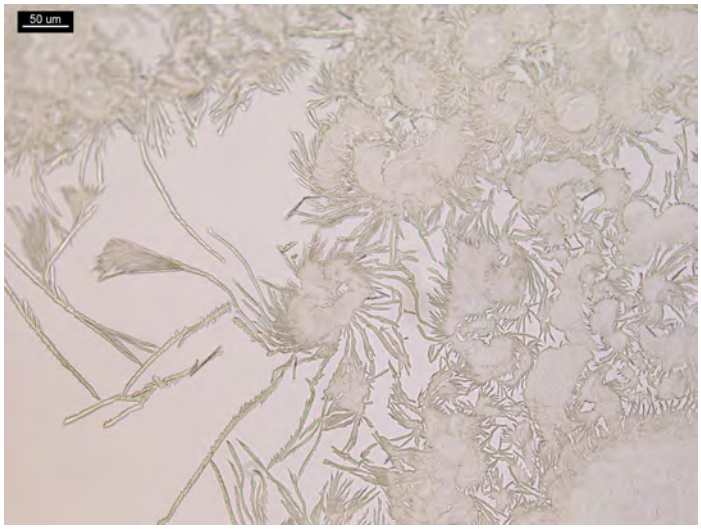

Figure 4. Direct test: 1 PPP of of *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Pinwheel and bushy rosettes appear on the top surface of the reagent drop.

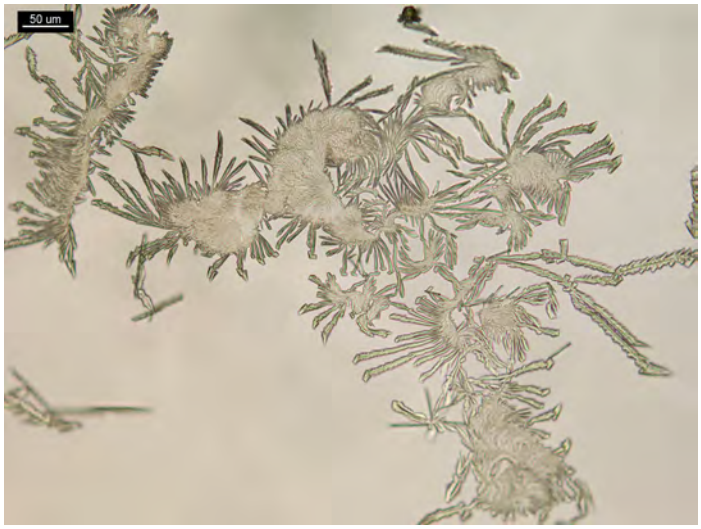

Figure 5. Direct test: 1 PPP of of *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Angular and dendritic crystals project from the pinwheel and bushy rosettes.

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d-Methamphetamine: Platinum Chloride (continued)

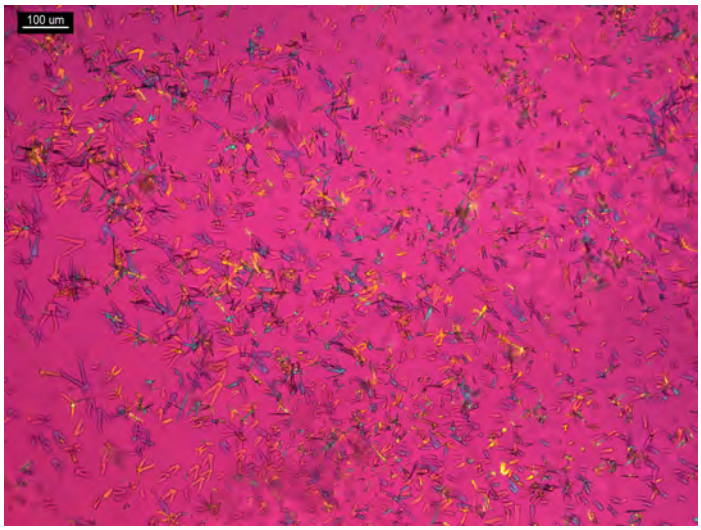

Figure 6. Direct test: Dimethylsulfone and *d*-methamphetamine (1:1) with 5 µL of H_2PtCl_6 reagent. Crystals form X shapes; crossed polars and Red I compensator.

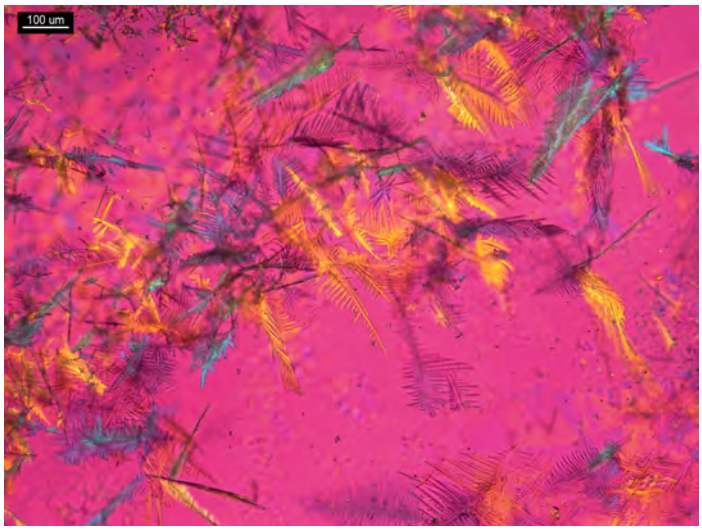

Figure 7. Direct test: Dimethylsulfone and *d*-methamphetamine (1:5) with 5 µL of H_2PtCl_6 reagent. Crystals form dendrites; crossed polars and Red I compensator.

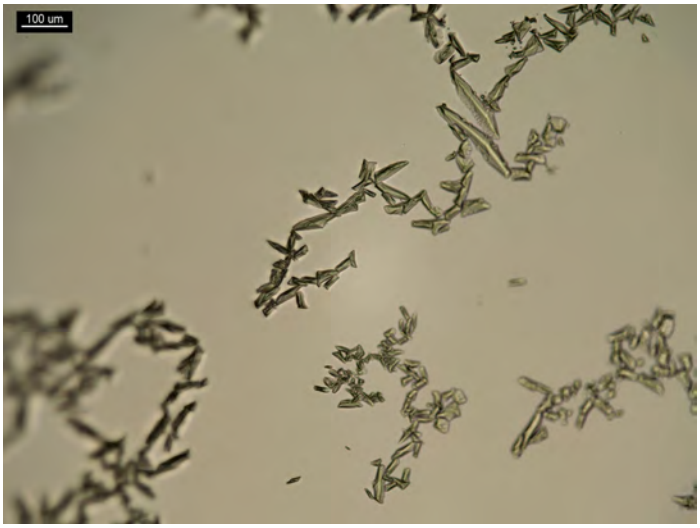

Figure 8. Volatility test: 1 PPP *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Crystals form triangular tablets and irregular plates.

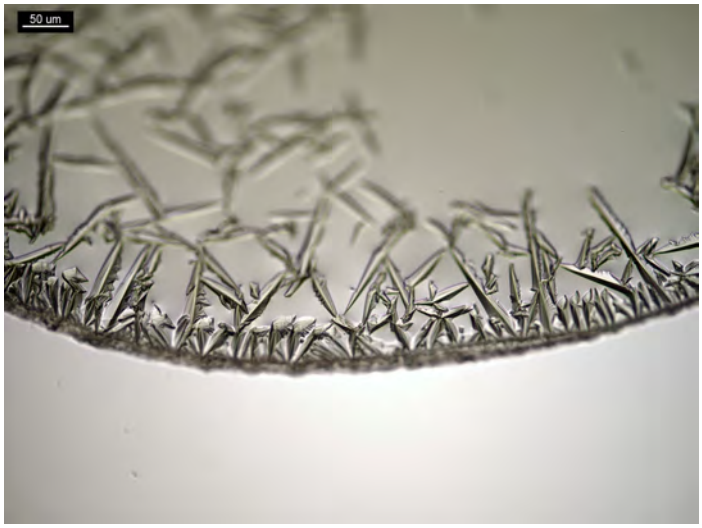

Figure 9. Volatility test: 1 PPP *d*-methamphetamine with 5 µL of H_2PtCl_6 reagent. Angular prisms appear at the edge of the drop.

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d-Methamphetamine: Platinum Chloride (continued)

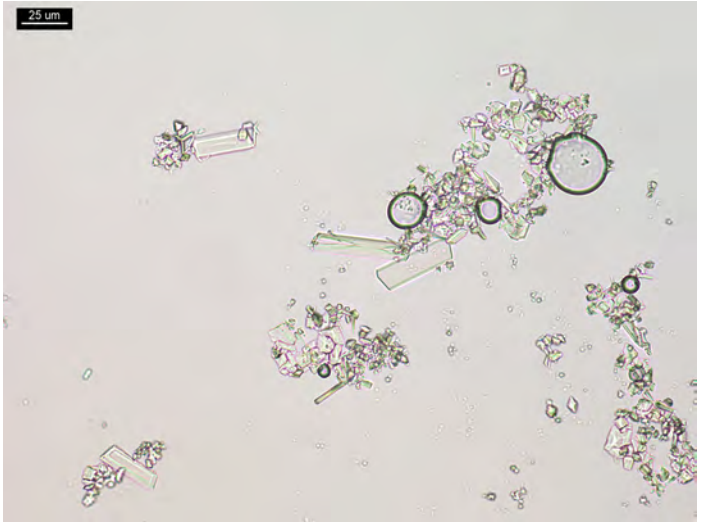

Figure 10. Volatility test: 1 PPP *d*-methamphetamine with 5 µL of H_2PtCl_6 and (1+3) H_3PO_4 reagent. Elongated prisms form over time.

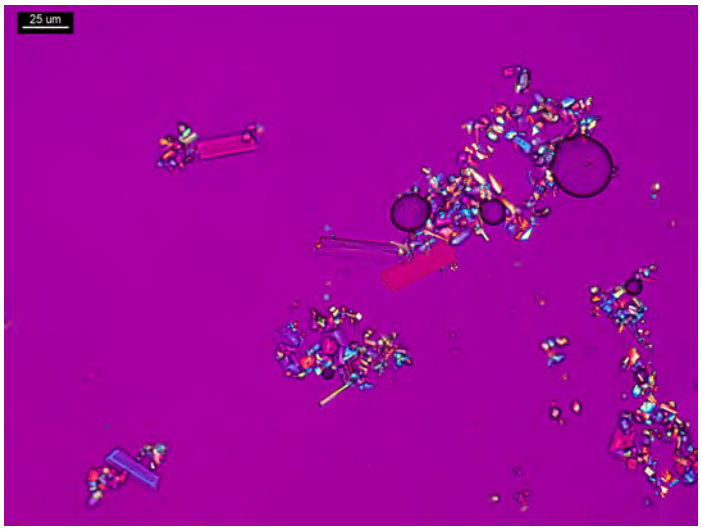

Figure 11. Same as Figure 10; crossed polars and Red I compensator.

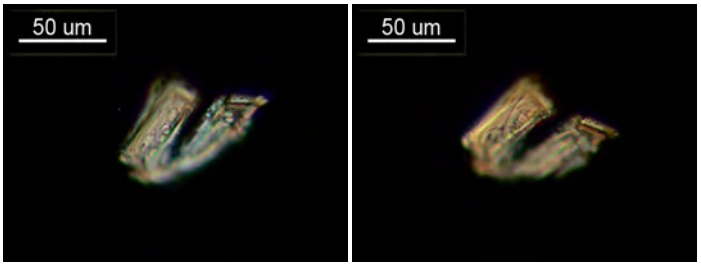

Figure 12. Direct test: 1 PPP of *d*-methamphetamine with 5 µL of H_2PtCl_6 and (1+3) H_3PO_4 reagent. Some views show dispersed extinction with interference colors changing from blue-gray to yellow during rotation of the stage.

Figure 13. Direct test: 1 PPP from a street drug sample of methamphetamine with 5 µL of H_2PtCl_6 and (1+3) H_3PO_4 reagent. Crystals form dendrites and X shapes.

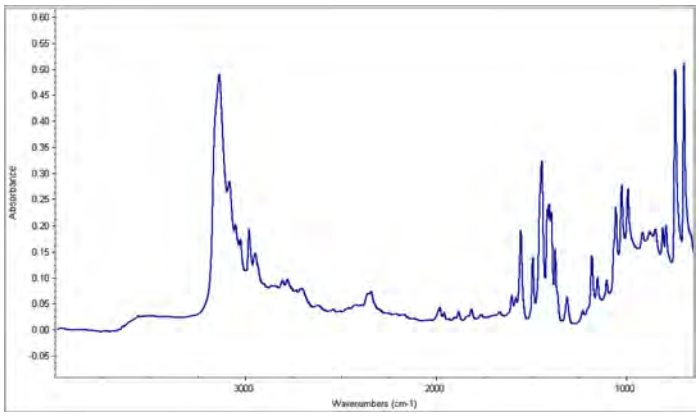

Figure 14. Infrared spectrum of *d*-methamphetamine platinum chloride precipitate. Download SPC file.

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dl-Methamphetamine: Gold Chloride

REAGENT 1: Gold Chloride ($HAuCl_4$)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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

There are two test methods: volatility and direct. Both produce the same crystals, however, the direct test is recommended because it is faster. **Direct test:** Add 5–10 µL of reagent directly to sample; gentle stirring is optional. Or, dissolve sample in 2 µL concentrated H_3PO_4 or (1+2) H_3PO_4, then add 5 µL of reagent. After formation of oily drops, gently mix drop with pipette tip, glass rod or toothpick to induce crystallization. **Volatility test:** With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL reagent drop on a coverslip, invert the coverslip and cover the glass ring for 5 minutes or until oily drops form at the edge of the hanging drop. Remove coverslip and place faceup to expose hanging drop to air. Gently mix drop with pipette tip, glass rod or toothpick to induce crystallization; typical crystals may not form without performing this step.

References

1. ASTM Designation E1969-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.
3. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Direct: Immediate, if the reagent is added directly to the sample. If the sample is first dissolved in concentrated H_3PO_4, crystals form instantly after mixing with pipette tip, glass rod or toothpick. **Volatility:** 5 minutes.

Crystal Morphology and Test Notes

Blunt, wide rectangular rods, usually narrower near their ends. Rods may also be indented. An X shape sometimes appears in the center of the rods. *dl*-Methamphetamine crystals are similar to *d*-methamphetamine crystals with the same gold chloride reagent, but *dl*-methamphetamine rods are not as forked or clothespin-like.

Photomicrograph of Typical Crystals

Figure 1. Direct test: 1 PPP of *dl*-methamphetamine and 5–10 µL of $HAuCl_4$ reagent. Rectangular rods with blunt or indented ends form instantly.

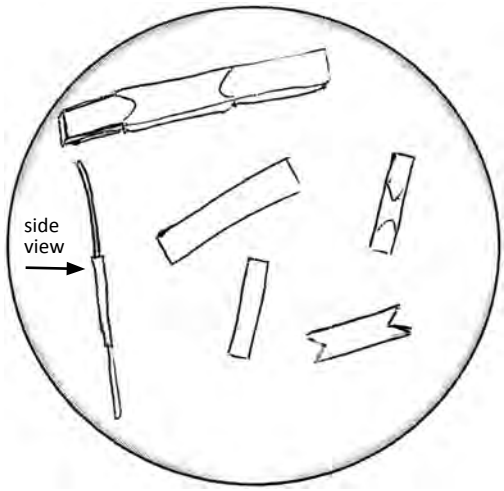
Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on street drug samples of *dl*-methamphetaine, including those adulterated with caffeine, dimethylsulfone or ephedrine. These common adulterants with *dl*-methamphetamine in ratios of 1:1 and 5:1 (adulterant:methamphetamine) had no apparent effect on this test.

PLM Optical Properties

Approximate Size Range	10 µm width, 75 µm length
Color/Pleochroism	Yellow. Pleochroic: colorless (parallel) to pale yellow (perpendicular); may not be apparent on thin crystals.
Refractive Indices (RI)	n-parallel ≈ 1.600 n-perpendicular > 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 RI liquid.
Estimated Birefringence	High
Extinction	Parallel on individual rods
Sign of Elongation	Negative (–)
Interference Figure	Indeterminable

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dl-Methamphetamine: Gold Chloride (continued)

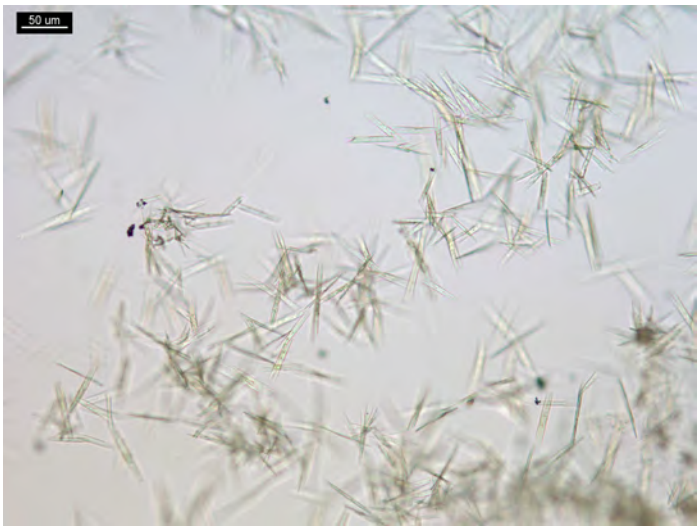

Figure 2. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of $HAuCl_4$ reagent. Blunt, rectangular rods are prevalent together with some indented rods having slight forks at both ends.

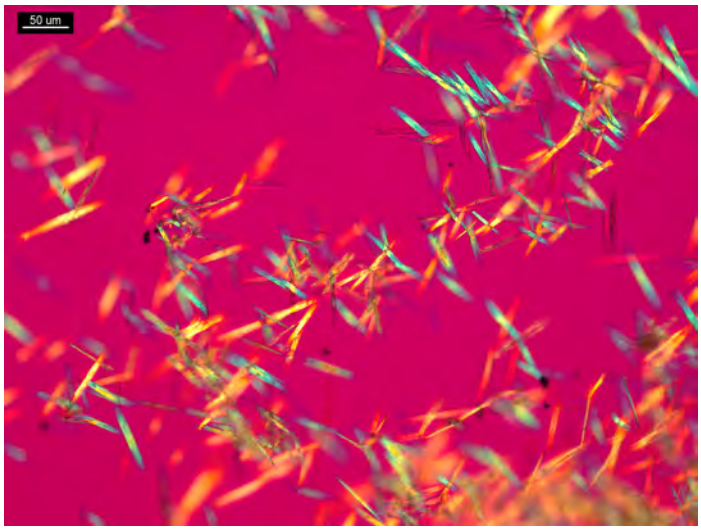

Figure 3. Same as Figure 2; crossed polars and Red I compensator.

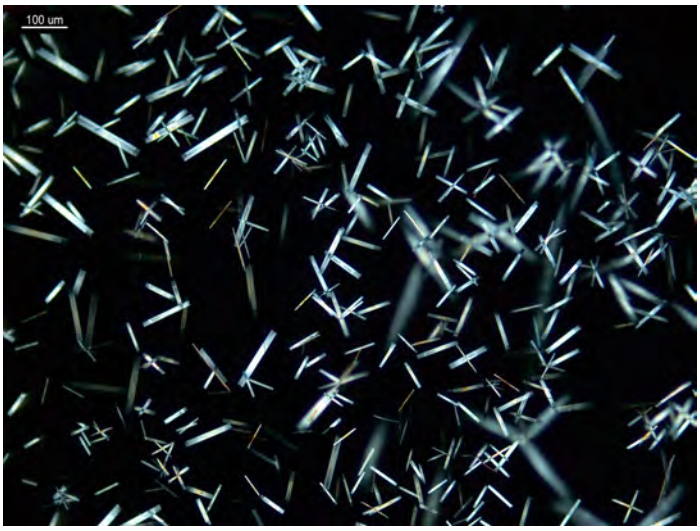

Figure 4. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of $HAuCl_4$ reagent. Rectangular rods with blunt or indented ends form instantly; crossed polars.

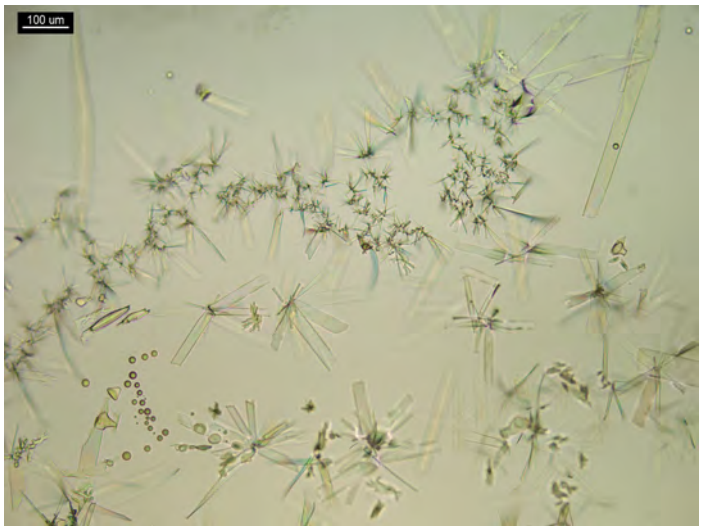

Figure 5. Volatility test: 1 PPP of *dl*-methamphetamine and 5 µL of $HAuCl_4$ reagent. The coverslip was removed from the reaction chamber, inverted, and the drop was mixed with a glass rod. Crystals grow instantly after mixing.

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dl-Methamphetamine: Gold Chloride (continued)

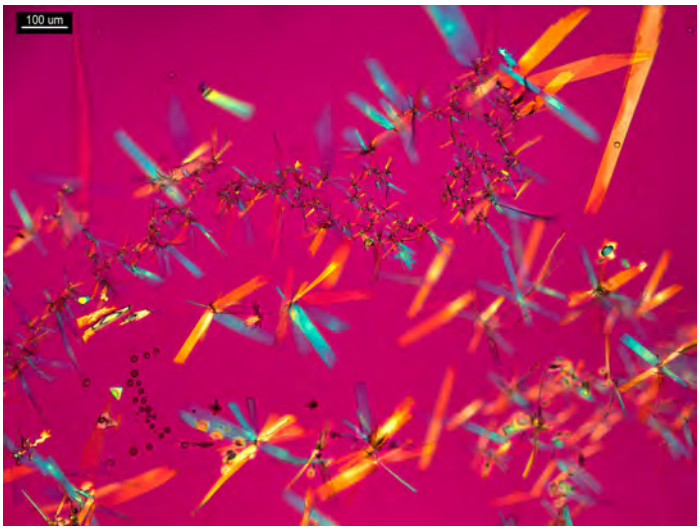

Figure 6. Same as Figure 5; crossed polars and Red I compensator.

Figure 7. Direct test: *dl*-Methamphetamine and caffeine (1:1) and 5 µL of $HAuCl_4$ reagent. Blunt, rectangular rods are prevalent together with some indented rods having slight forks at both ends. Caffeine had no apparent effect on this test.

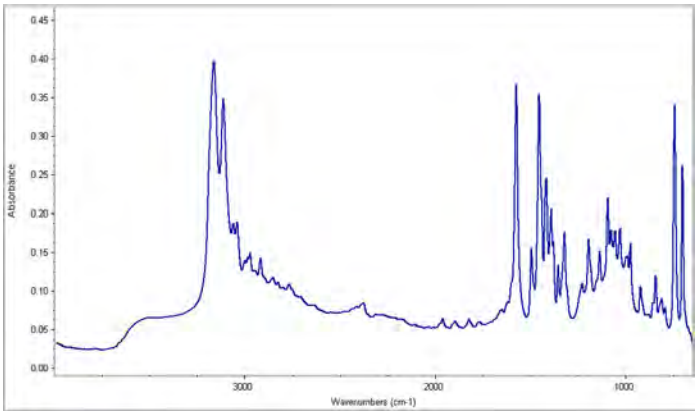

Figure 8. Infrared spectrum of *dl*-methamphetamine gold chloride precipitate. Download SPC file.

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dl-Methamphetamine: Platinum Chloride

REAGENT 2: Platinum Chloride (H_2PtCl_6)

There are two reagents; both produce the same crystals: **1 g $H_2PtCl_6 \cdot 6H_2O$ in (1+3) H_3PO_4,** make up to 20 mL. (1+3) H_3PO_4 is dilute phosphoric acid made by combining one part (e.g. 5 mL) of concentrated phosphoric acid with three parts (e.g. 15 mL) of water (direct or volatility test methods). **5% aqueous:** 1 g $H_2PtCl_6 \cdot 6H_2O$ in H_2O, make up to 20 mL (direct test method only)

Test Method

There are two test methods: direct and volatility; each produce different crystals. **Direct test:** Dissolve sample in 5 µL concentrated H_3PO_4, then add 5 µL of reagent to the edge of the acid drop; crystals form instantly. **Volatility test:** With a glass ring placed on a glass slide and the sample at its center, add a drop of 10 N NaOH (40%). Then, with a 5 µL H_2PtCl_6 and (1+3) H_3PO_4 drop on a coverslip, invert the coverslip and cover the glass ring for 5 minutes or until crystals begin to form.

References

1. ASTM Designation E1969-11: Standard Guide for Microcrystal Testing in Forensic Analysis of Methamphetamine and Amphetamine, ASTM International: West Conshohocken, PA, 2011.
2. AOAC Official Methods. 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.
3. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Direct: Immediate **Volatility:** < 5 minutes

Crystal Morphology and Test Notes

dl-Methamphetamine crystals are similar to *d*-methamphetamine crystals with the same platinum chloride reagent.
Direct: Dendrites, feathery X-shaped crystals, stars and some bushy pinwheel rosettes. Six-sided prisms form over time.
Volatility: Rectangular pyramids, rice grains and rods.

Photomicrograph of Typical Crystals

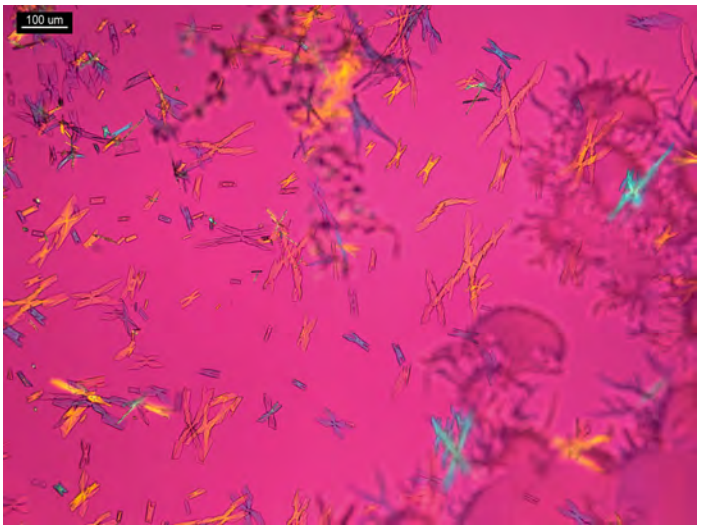


Figure 1. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Dendrites, X-shaped crystals and some short rods form instantly.

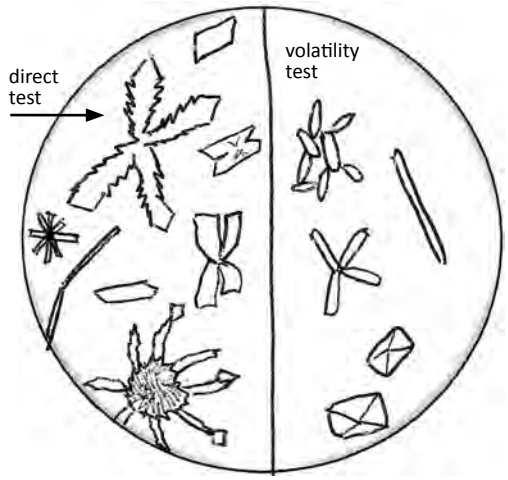
Pharmaceuticals, Adulterants or Other Drug Interactions

This test worked well on street drug samples of *dl*-metham phetamine, including those adulterated with caffeine, dimethylsulfone or ephedrine. These common adulterants with *dl*-methamphetamine in ratios of 1:1 and 5:1 (adulterant: methamphetamine) had no apparent effect on this test.

PLM Optical Properties

Approximate Size Range	**Direct:** 5 µm width, 100 µm length; length can be > 300 µm **Volatility:** 5–50 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	All RIs > 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 RI liquid.
Estimated Birefringence	Moderate
Extinction	Prisms: parallel and symmetrical Pinwheel rosettes: undulose Some X-shaped crystals showed dispersed extinction (blue-gray to pale yellow)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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dl-Methamphetamine: Platinum Chloride (continued)

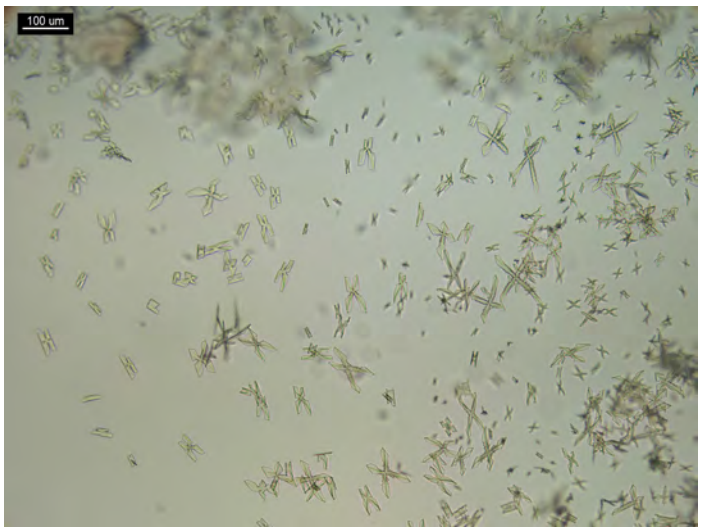

Figure 2. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Crystals form X shapes.

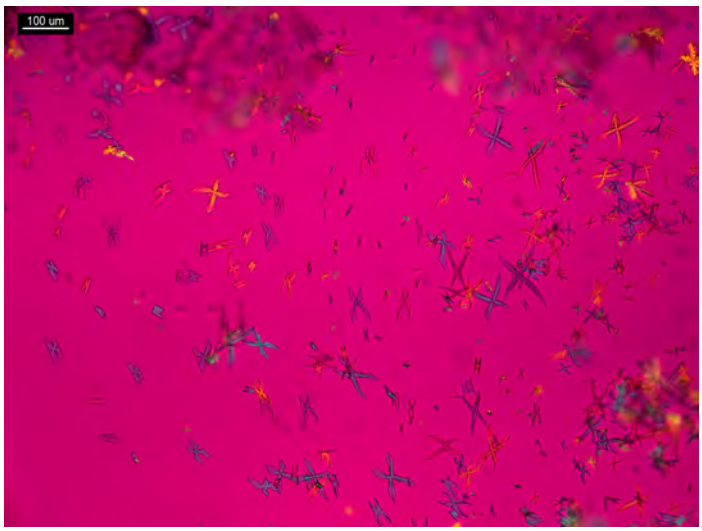

Figure 3. Same as Figure 2; crossed polars and Red I compensator.

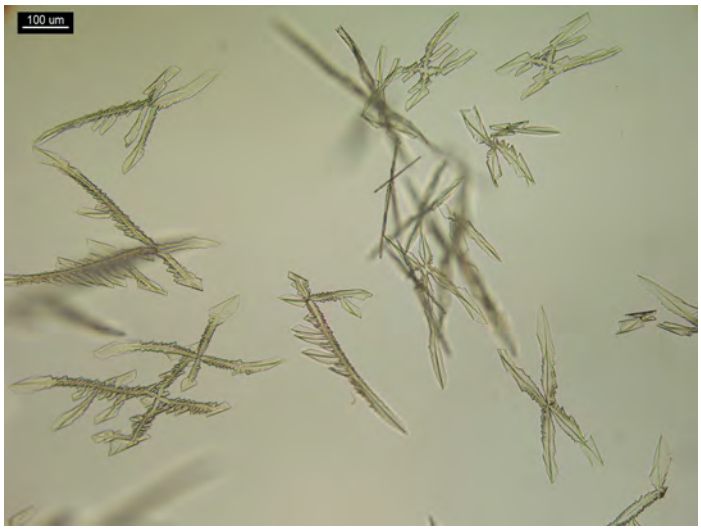

Figure 4. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Crystals form feathery X shapes.

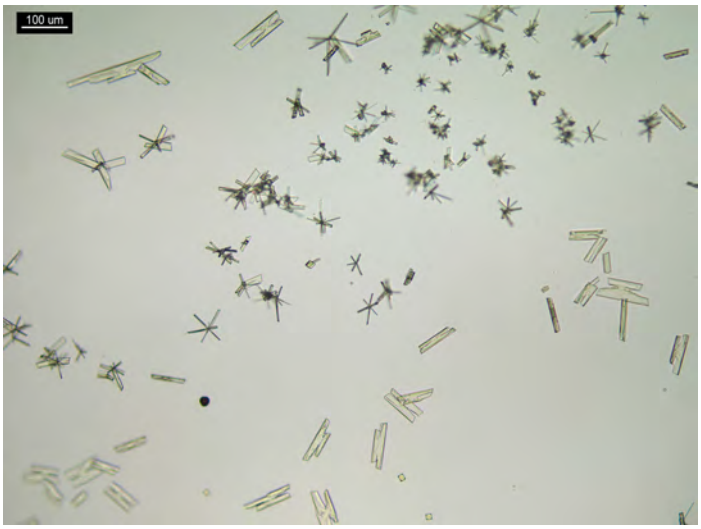

Figure 5. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Crystals form rods and stars.

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dl-Methamphetamine: Platinum Chloride (continued)

Figure 6. Direct test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Crystals form bushy pinwheel rosettes; crossed polars and Red I compensator.

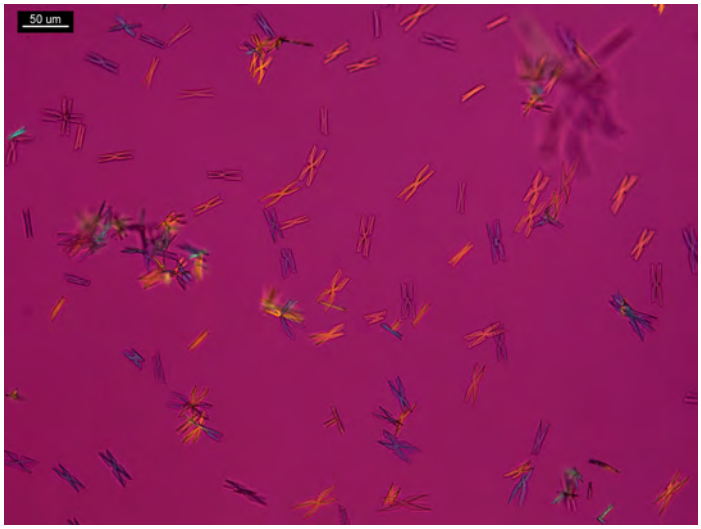

Figure 7. Direct test: *dl*-Methamphetamine and caffeine (1:5) and 5 µL of H_2PtCl_6 reagent. Feathery X-shaped crystals are prevalent. Caffeine had no apparent effect on this test.

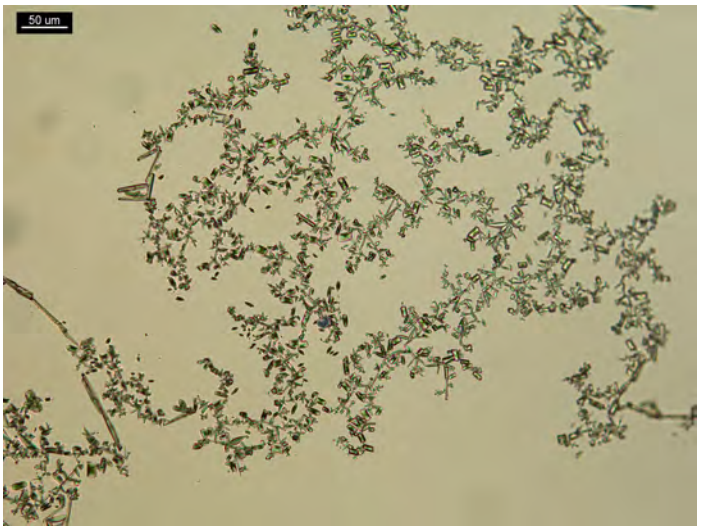

Figure 8. Volatility test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Rectangular pyramids, rice grains and rods form in clusters. For this photomicrograph, the coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide.

Figure 9. Volatility test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Rice grains and rods form in clusters. For this photomicrograph, the coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide; crossed polars and Red I compensator.

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dl-Methamphetamine: Platinum Chloride (continued)

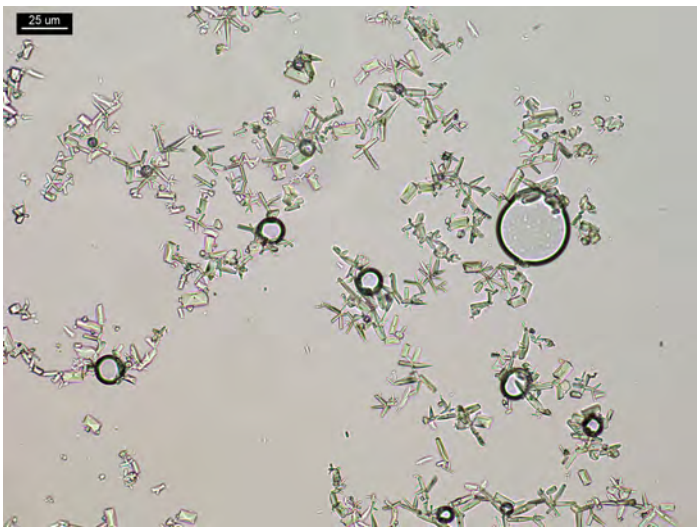

Figure 10. Volatility test: 1 PPP of *dl*-methamphetamine and 5 µL of H_2PtCl_6 reagent. Rectangular pyramids, rice grains and rods form in clusters. For this photomicrograph, the coverslip with the hanging drop was removed from the reaction chamber and placed facedown onto the glass slide.

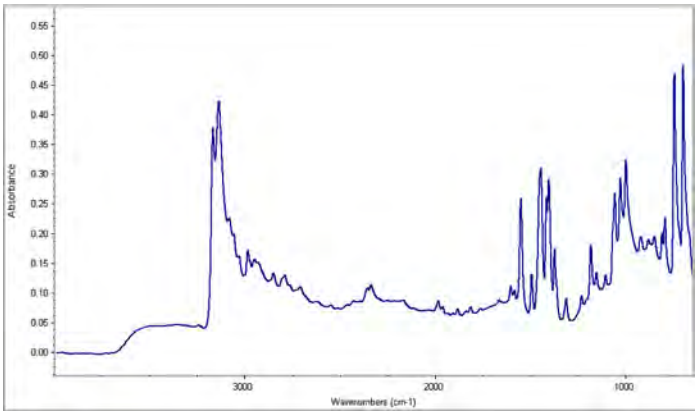

Figure 11. Infrared spectrum of *dl*-methamphetamine platinum chloride precipitate. Download SPC file.

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Methylphenidate: Picric Acid

REAGENT 1: Picric Acid ($C_6H_2(NO_2)_3OH$)

Picric acid, saturated aqueous solution

Test Method

Direct test: Add 10 µL of reagent directly to sample on a glass slide; coverslip optional.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

3–10 minutes

Crystal Morphology and Test Notes

Rosettes of plates, plate clusters, pinwheel-shaped crystals, elongated prisms, sheaves, stars and dendrites.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of methylphenidate and 10 µL of picric acid reagent. Crystals form rosettes of plates.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 mg, 20 mg and 54 mg tablets. The 54 mg tablet was two-tone (white/brown); only the white portion produced crystals. A test of a Daytrana® transdermal patch containing 27.5 mg of methylphenidate was successful after an ethanol extraction: 2 PPP of the drug-containing adhesive was removed from the patch and placed on a glass slide. A 10 µL drop of ethanol was added then extracted with a tungsten needle. After the ethanol evaporated, the direct test was performed. Alternatively, a 5 mm square of the patch drug material was cut out, placed into a microcentrifuge tube with 100 µL of ethanol, then allowed to sit for 3 minutes. 20 µL was placed onto a glass slide and tested directly. A test of an oral solution containing 1 mg/mL methylphenidate was successful after a chloroform extraction: 100 µL of the oral solution and 100 µL of chloroform were placed into a microcentrifuge tube, mixed with a pipette tip, then allowed to sit for 1 minute until a cloudy layer formed. 10 µL of the cloudy layer was dropped onto a glass slide and tested directly.

PLM Optical Properties

Approximate Size Range	Rosettes: 50–150 µm; Plates: 10–30 µm width, 30–100 µm length; Needles: 5–10 µm width, > 100 µm length
Color/Pleochroism	Colorless to pale yellow; not pleochroic
Refractive Indices (RI)	> 1.500. Soluble in 1.660 and 1.700 RI liquids.
Morphology Illustration	*not to scale*
How Crystals Were Dried for RI Measurement	Crystals were gently heated.
Estimated Birefringence	High
Extinction	Clusters: incomplete; Individual rectangular plates: parallel
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

Note: Methylphenidate and tramadol with the picric acid reagent form crystals that are indistinguishable. Therefore, the lead iodide solution reagent should be used for methylphenidate (page 107).

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Methylphenidate: Picric Acid (continued)

Figure 2. 1 PPP of methylphenidate and 10 µL of picric acid reagent. Crystals form sheaves, stars and dendrites.

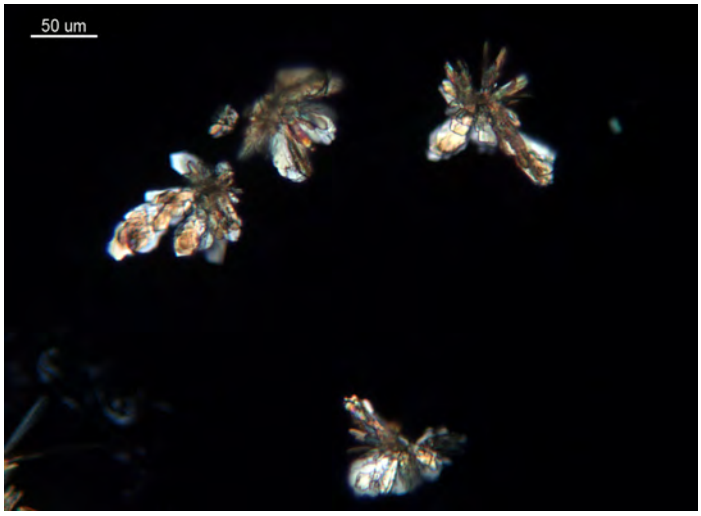

Figure 3. Same as Figure 2; crossed polars .

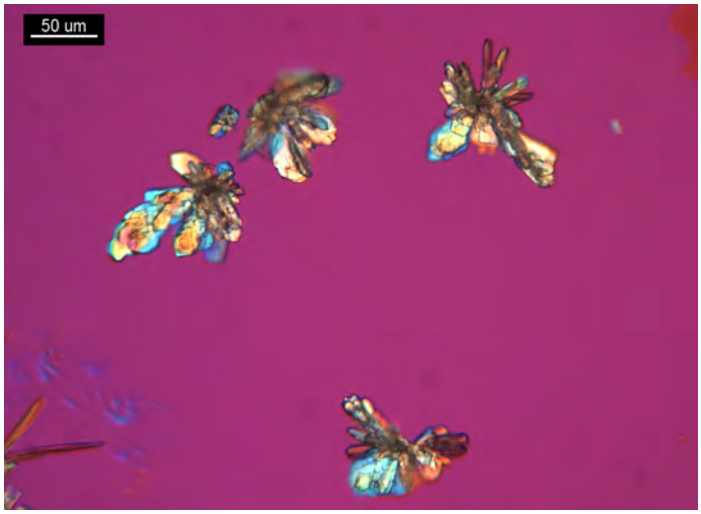

Figure 4. Same as Figure 2; crossed polars and Red I compensator.

Figure 5. 1 PPP of methylphenidate from a 5 mg tablet and picric acid reagent. Crystals form pinwheel shapes.

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Methylphenidate: Picric Acid (continued)

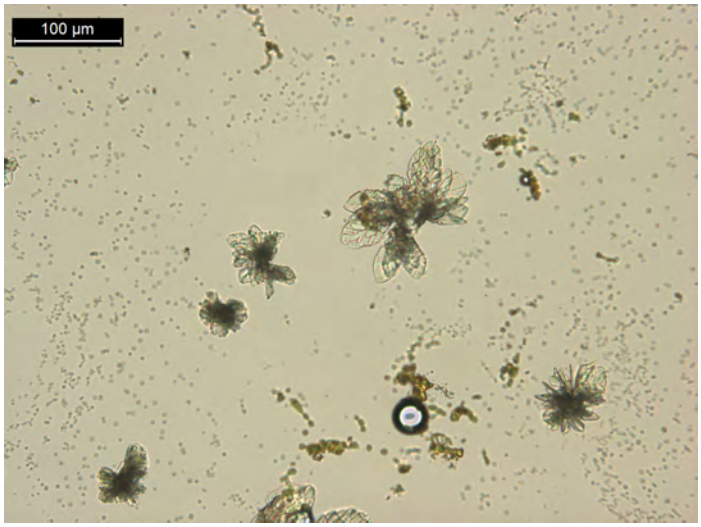

Figure 6. 1 PPP of methylphenidate from a 20 mg tablet and picric acid reagent. Crystals form rosettes of plates and plate clusters.

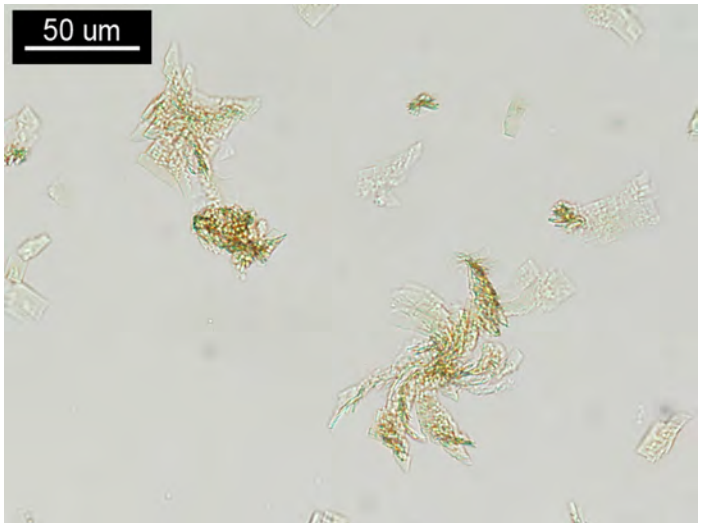

Figure 7. 1 PPP of methylphenidate from a 54 mg tablet and picric acid reagent. Crystals form pinwheel shapes.

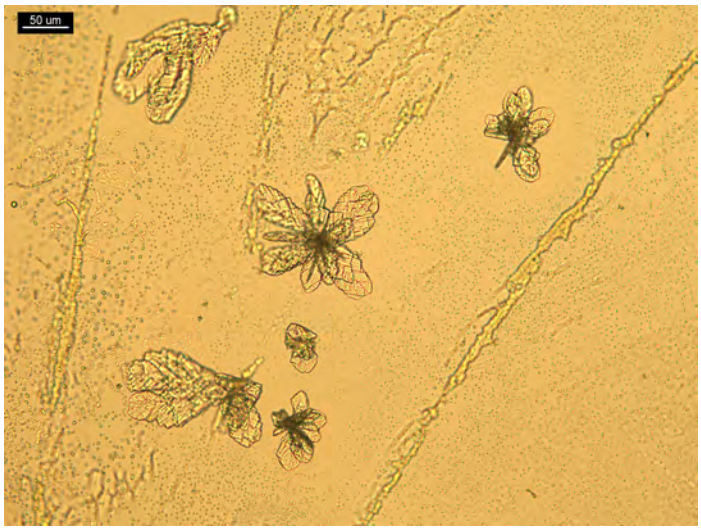

Figure 8. 2 PPP of the drug material from a Daytrana® transdermal patch containing 27.5 mg of methylphenidate and picric acid reagent, after ethanol extraction. Crystals form rosettes of plates and plate clusters.

Figure 9. 10 µL from a methylphenidate oral solution (1 mg/mL) after chloroform extraction and 10 µL of picric acid reagent. Crystals form pinwheel shapes.

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Methylphenidate: Picric Acid (continued)

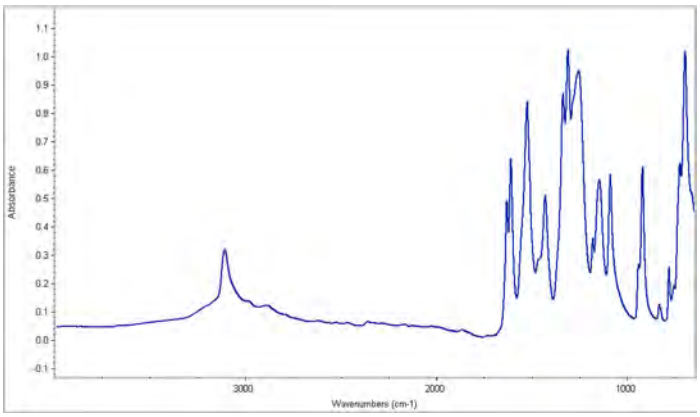

Figure 10. Infrared spectrum of methylphenidate picric acid precipitate. Download SPC file.

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Methylphenidate: Lead Iodide Solution

REAGENT 2: Lead Iodide (PbI_2) Solution

30% potassium acetate (KCH_3COO) in H_2O (adjust the pH to 6.0 by adding 2 N HOAc), then fully saturate with PbI_2. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Add 10 µL of reagent directly to sample on a glass slide; coverslip optional.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

3 PPP

Time Required for Crystal Formation

1–5 minutes

Crystal Morphology and Test Notes

Small burrs that develop into large rosettes of blades and clusters can resemble dahlia flowers.

Photomicrograph of Typical Crystals

Figure 1. 3 PPP of methylphenidate and 10 µL of lead iodide solution reagent. Crystals form large rosettes of blades and clusters.

Pharmaceuticals, Adulterants or Other Drug Interactions

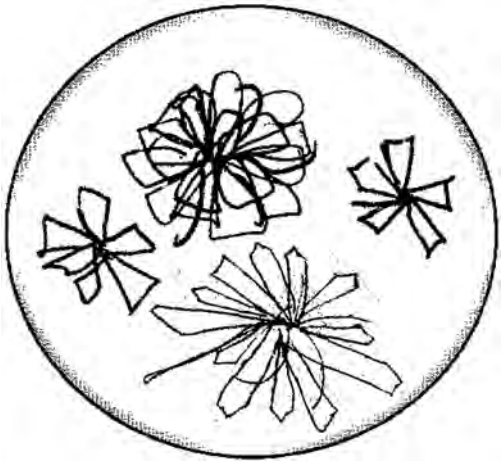
This test was successful on 5 mg, 20 mg and 54 mg tablets. The 54 mg tablet was two-tone (white/brown); only the white portion produced crystals. A test of a Daytrana® transdermal patch containing 27.5 mg of methylphenidate was successful after an ethanol extraction: 2 PPP of the drug-containing adhesive was removed from the patch and placed on a glass slide, a 10 µL drop of ethanol was added then extracted with a tungsten needle. After the ethanol evaporated, the direct test was performed. An oral solution containing 1 mg/mL of methylphenidate gave inconclusive results: rosettes of thin, straight rods.

Note: This microcrystal test distinguishes between methylphenidate and tramadol. With the lead iodide solution reagent, methylphenidate forms rosettes of blades and clusters (Figure 1); tramadol forms rods and stars of rods (Figure 9).

PLM Optical Properties

Approximate Size Range	100 µm up to >1 mm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	>1.700

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then washed with RI liquid.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 10. Download SPC file.

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Methylphenidate: Lead Iodide Solution (continued)

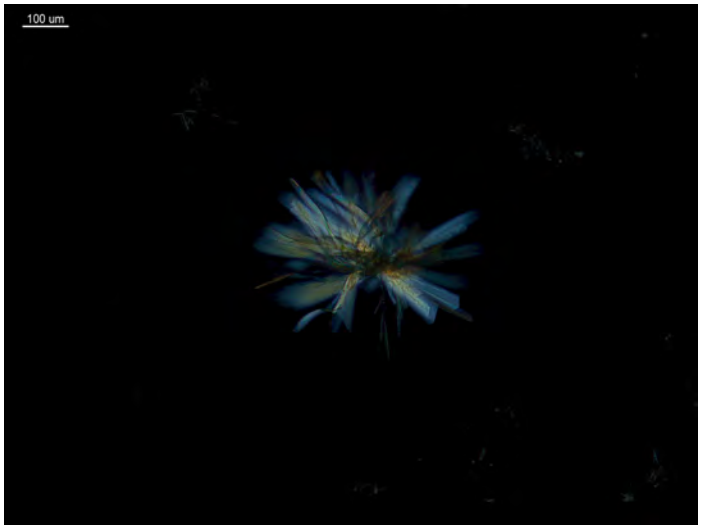

Figure 2. Same as Figure 1; crossed polars.

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

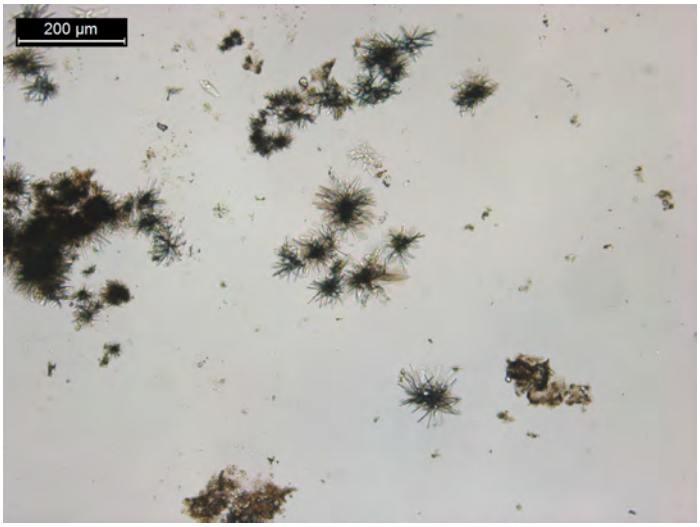

Figure 4. 3 PPP from a 5 mg methylphenidate tablet and 10 µL of lead iodide solution reagent. Crystals form rosettes of blades.

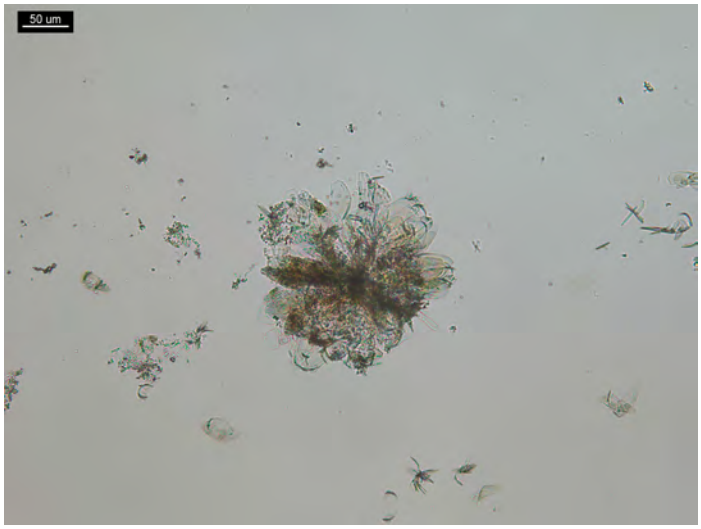

Figure 5. 3 PPP from a 20 mg methylphenidate tablet and 10 µL of lead iodide solution reagent. Crystals form a cluster of blades.

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Methylphenidate: Lead Iodide Solution (continued)

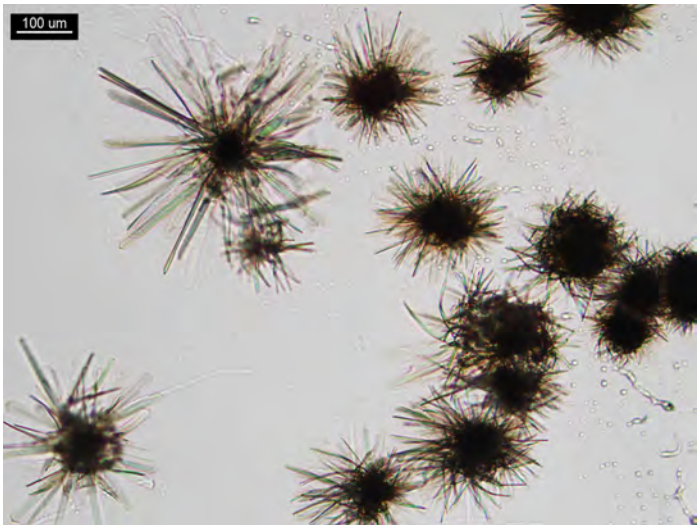

Figure 6. 2 PPP of the drug-containing adhesive from a Daytrana® transdermal patch containing 27.5 mg of methylphenidate and 10 µL of lead iodide solution reagent, after ethanol extraction. Crystals form rosettes of blades.

Figure 7. 10 µL from a methylphenidate oral solution (1 mg/mL) after chloroform extraction and 10 µL of lead iodide solution reagent. Results are inconclusive because rosettes of rods, rather than blades, formed.

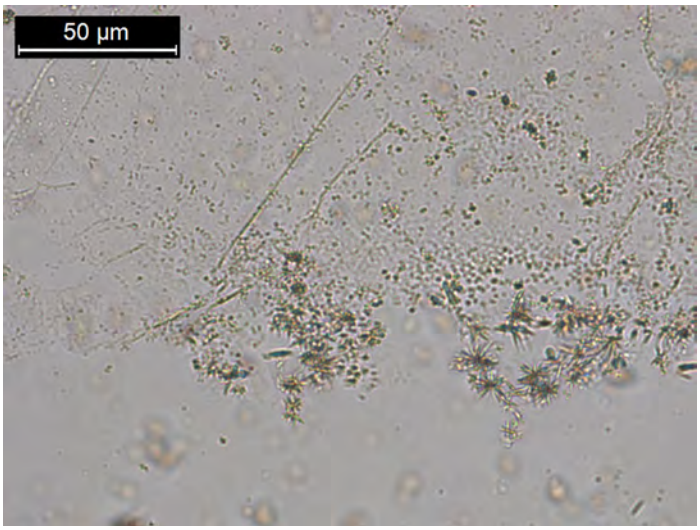

Figure 8. 2 PPP from a 54 mg methylphenidate tablet and 10 µL of lead iodide solution reagent. Crystals form rosettes of blades.

Figure 9. 3 PPP of tramadol and 10 µL of lead iodide solution reagent. Crystals form rods and stars of rods, which are distinguishable from methylphenidate.

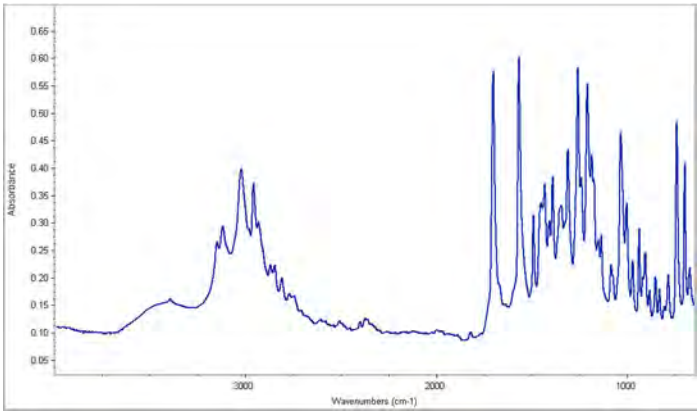

Figure 10. Infrared spectrum of methylphenidate lead iodide solution precipitate. Download SPC file.

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Morphine: Gold Bromide

REAGENT 1: Gold Bromide ($HAuBr_4$)

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: Place sample on glass slide. Add 10 µL drop of reagent on a coverslip, invert the coverslip and place it directly onto the sample. Do not stir the sample or apply any pressure to the coverslip, otherwise small, slow-growing crystals will form.

References

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

Limit of Detection

1 PPP

Time Required for Crystal Formation

1–10 minutes (pharmaceutical solutions up to ≈ 20 minutes)

Crystal Morphology and Test Notes

Plates, layers of plates, clusters of plates and rosettes of plates, burrs of blades and needles.

Photomicrograph of Typical Crystals

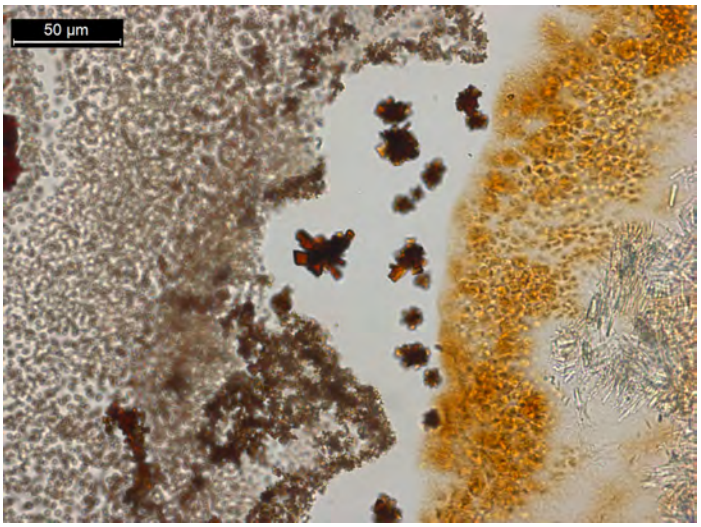

Figure 1. 1 PPP of morphine and 10 µL of $HAuBr_4$ reagent. Clusters of plates (center), oily drops (left) and undissolved morphine (right) are visible.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 15 mg, 30 mg (extended release), 60 mg (extended release) and 100 mg morphine pharmaceutical tablets. 1 PPP of material from the inner portion of the tablet was used, but it may require up to 10 minutes for typical crystal formation. This test was also successful on a 20 mg/mL morphine sulfate oral solution and formed small, dense burrs or rosettes of blades.

IR Spectrum

See Figure 9. Download SPC file.

PLM Optical Properties

Approximate Size Range	10 to > 60 µm
Color/Pleochroism	Red-orange. Pleochroic: colorless to orange or red
Refractive Indices (RI)	n_1 > 1.700 (red orientation) n_2 ≈ 1.640 (colorless or orange orientation)

Morphology Illustration

not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then washed with water and dried at room temperature.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Morphine: Gold Bromide (continued)

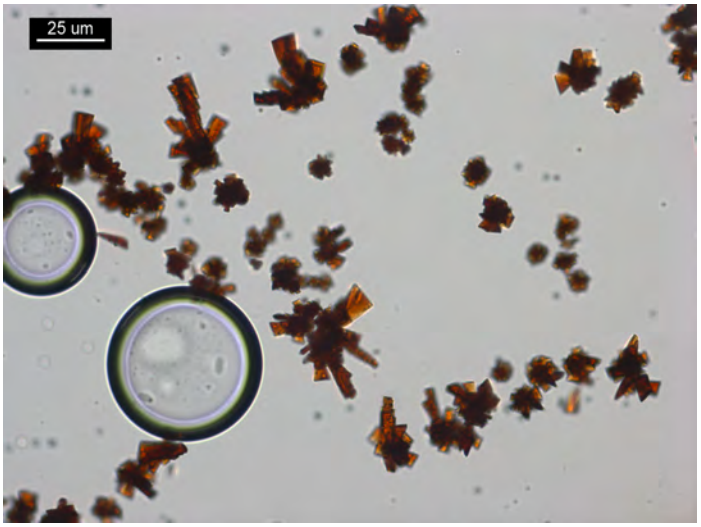

Figure 2. 1 PPP of morphine and 10 µL of $HAuBr_4$ reagent. Crystals form clusters and rosettes of plates. Pleochroism on plates: red to orange; East-West polarizer.

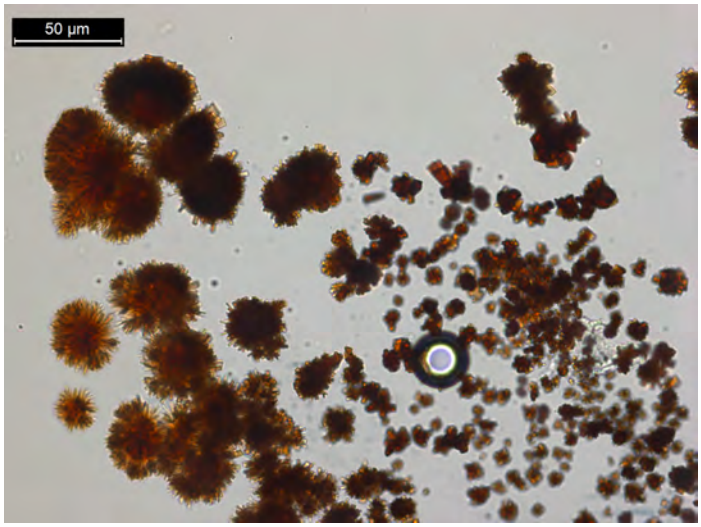

Figure 3. 1 PPP of morphine and 10 µL of $HAuBr_4$ reagent. Crystals form clusters of plates and needles.

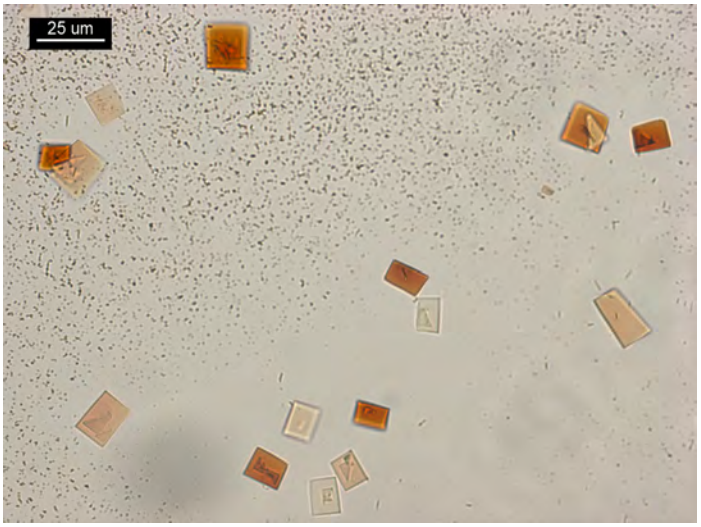

Figure 4. 1 PPP of morphine and 10 µL of $HAuBr_4$ reagent. Crystals form pleochroic (nearly colorless to orange) plates.

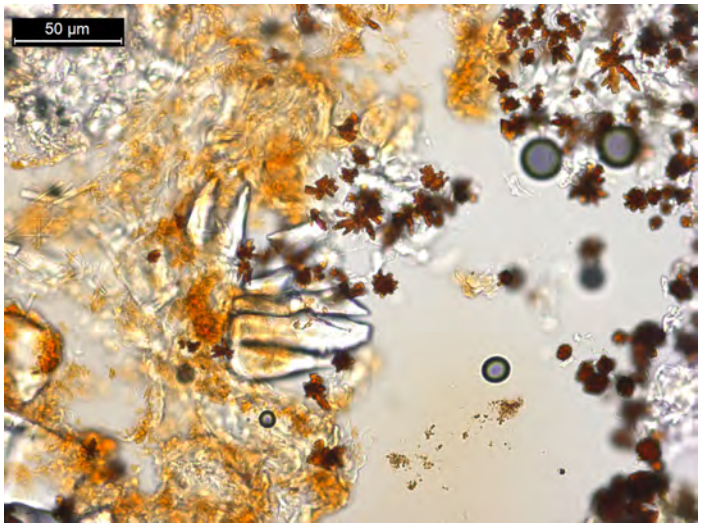

Figure 5. 1 PPP from a 60 mg morphine (extended release) pharmaceutical tablet and 10 µL of $HAuBr_4$ reagent. Crystals form clusters and rosettes of plates.

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Morphine: Gold Bromide (continued)

Figure 6. 2 PPP from a 30 mg morphine (extended release) pharmaceutical tablet and 10 µL of $HAuBr_4$ reagent form plates and rosettes of plates.

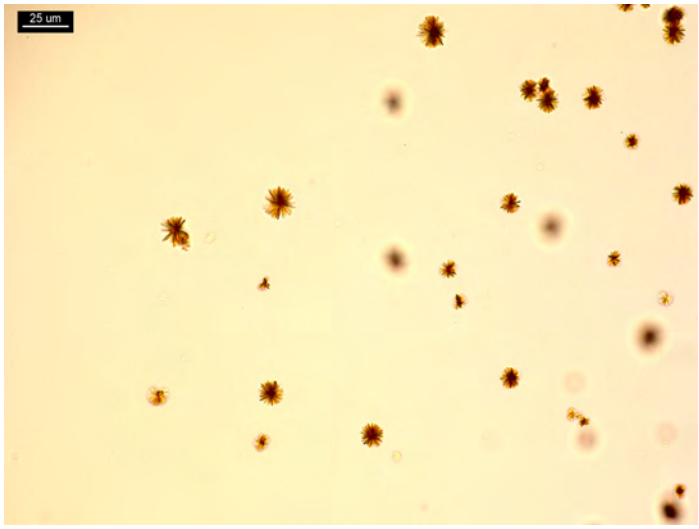

Figure 7. 5 µL from a morphine sulfate oral solution (20 mg/mL) and 10 µL of $HAuBr_4$ reagent form rosettes of blades.

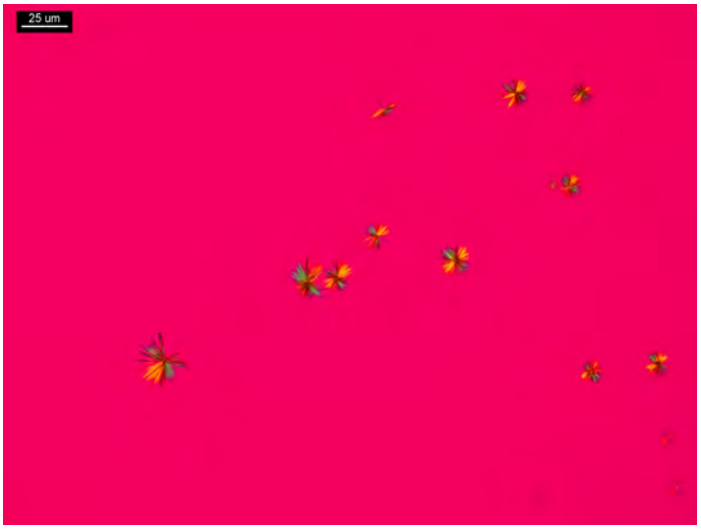

Figure 8. 5 µL from a morphine sulfate oral solution (20 mg/mL) and 10 µL of $HAuBr_4$ reagent form rosettes of blades with a negative sign of elongation; crossed polars and Red I compensator.

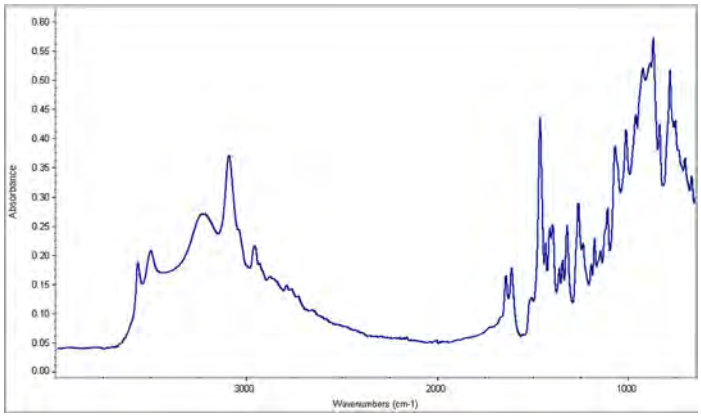

Figure 9. Infrared spectrum of morphine gold bromide precipitate. Download SPC file.

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Morphine: Wagner's Reagent (I-KI)

REAGENT 2: Wagner's Reagent (I-KI)

1 g I_2 and 5 g of KI in H_2O, make up to 100 mL. Reagent does not keep and should be fresh when used.

Test Method

Direct test: Dissolve sample in 5 µL of water, then add 5 µL of reagent. Stir for 30 seconds with a pipette tip, glass rod or toothpick; stirring the drop is required.

References

1. Stephenson, C.H. *Microchemical Tests for Alkaloids*, Charles Griffin & Co., Ltd.: London, 1921.

Limit of Detection

1 PPP (High humidity may require up to 3 PPP.)

Time Required for Crystal Formation

≈ 1 minute

Crystal Morphology and Test Notes

Thin irregular plates (some 90° angles) and feathery plates. Fuzzy dendrites form at the edge of the drop.

Photomicrograph of Typical Crystals

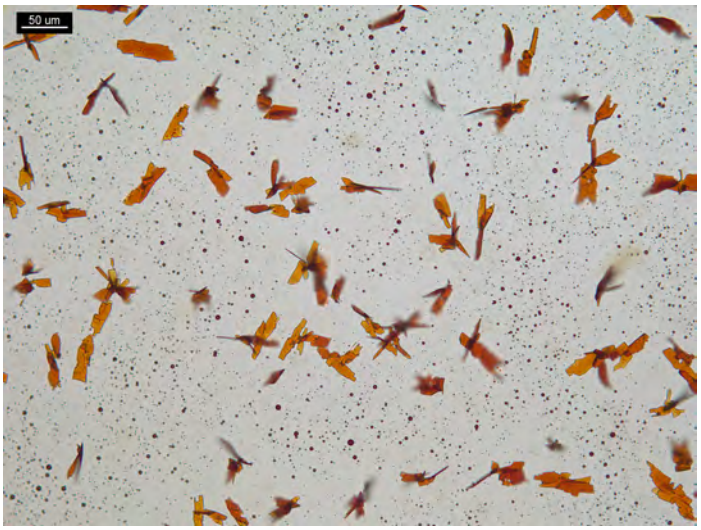


Figure 1. 3 PPP of morphine in 5 µL of water and 5 µL of Wagner's I-KI reagent form thin, irregular plates.

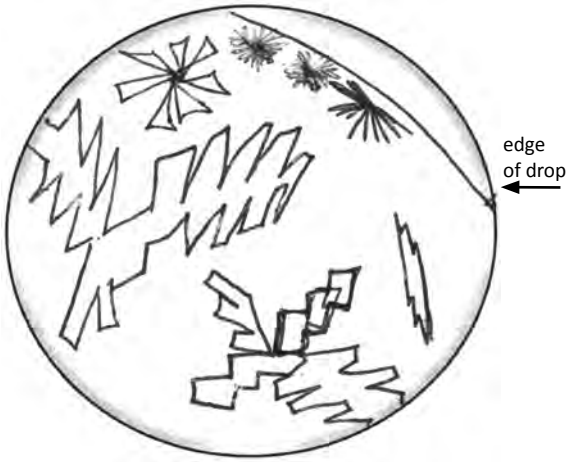
Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on a 20 mg/mL morphine sulfate oral solution, without an acid-base extraction: 5 µL from an oral solution (20 mg/mL) and 5 µL of $HAuBr_4$ reagent formed typical crystals immediately after 30 seconds of stirring. This test was not always successful or reproducible with morphine pharmaceutical tablets.

IR Spectrum

See Figure 6. Download SPC file.

PLM Optical Properties

Approximate Size Range	> 20 µm
Color/Pleochroism	Red-brown. Pleochroic: red-brown to red-orange
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 filter paper.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Not applicable
Crystal Optics and Optic Sign (Interference Figure)	Biaxial; optic sign indeterminable

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Morphine: Wagner's I-KI (continued)

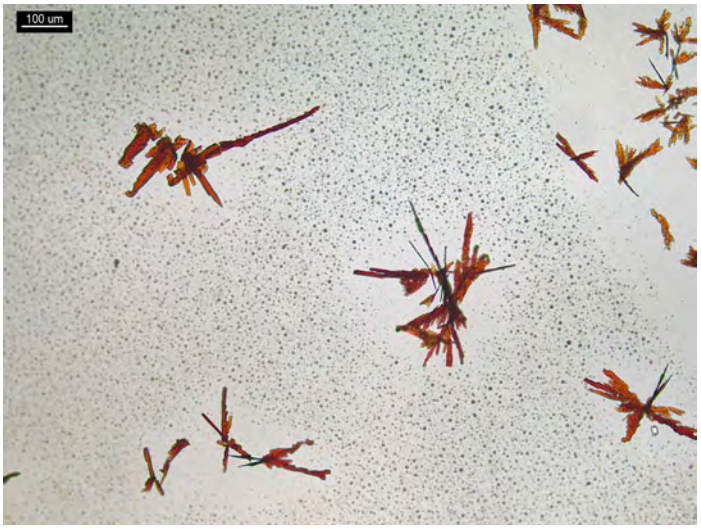

Figure 2. 3 PPP of morphine in 5 µL of water and 5 µL of Wagner's I-KI reagent. Crystals form clusters of irregular, feathery plates.

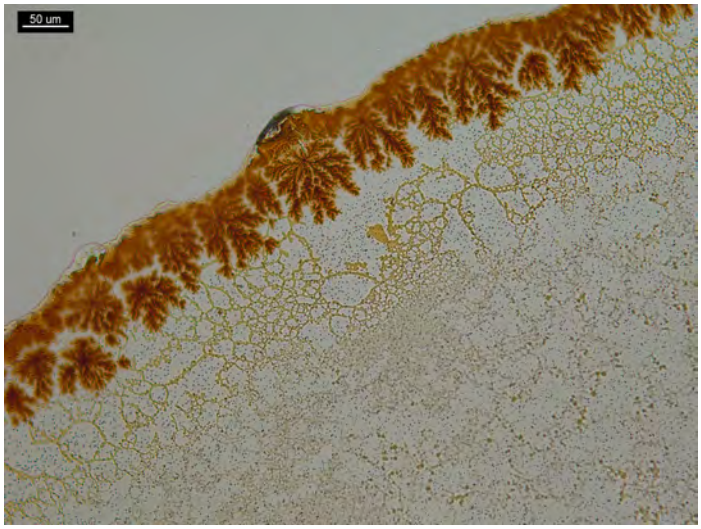

Figure 3. 3 PPP of morphine in 5 µL of water and 5 µL of Wagner's I-KI reagent. Fuzzy dendrites form at the edge of the drop.

Figure 4. 3 PPP of morphine in 5 µL of water and 5 µL of Wagner's I-KI reagent. Crystals form clusters of irregular, feathery plates.

Figure 5. Dried Wagner's I-KI reagent only (no morphine).

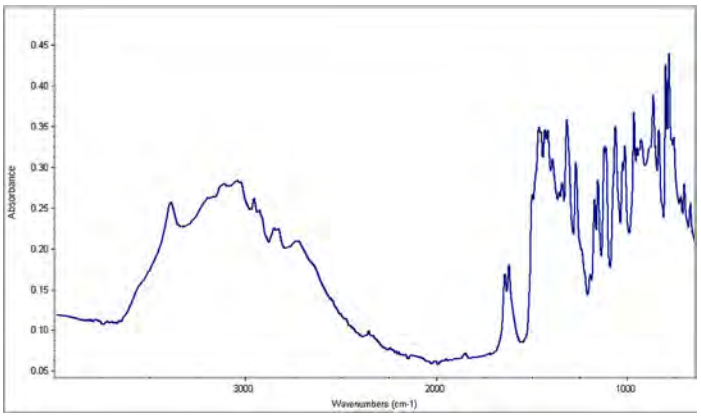

Figure 6. Infrared spectrum of morphine Wagner's I-KI precipitate. Download SPC file.

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Morphine: Mercuric Chloride

REAGENT 3: Mercuric Chloride ($HgCl_2$)

5% aqueous: 5 g $HgCl_2$ in H_2O, make up to 100 mL

Test Method

Direct test: Dissolve sample in 5 µL of reagent and stir with a pipette tip, glass rod or toothpick.

References

1. Stephenson, C.H. *Microchemical Tests for Alkaloids*, Charles Griffin & Co., Ltd.: London, 1921.

Limit of Detection

1 PPP (3 PPP for pharmaceutical tablets)

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Dense rosettes of needles form immediately. After several minutes, the crystals become overgrown with large blades and are no longer recognizable.

Photomicrograph of Typical Crystals

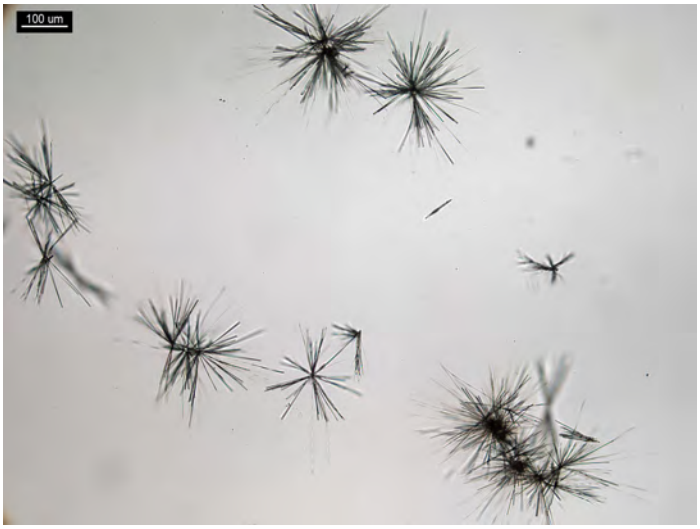


Figure 1. 5 PPP of morphine and 5 µL of $HgCl_2$ reagent form rosettes of needles.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 15 mg and 100 mg morphine pharmaceutical tablets using 3 PPP of material from the inner portion of the tablet. This test was unsuccessful with 30 mg (extended release), 60 mg (extended release) morphine pharmaceutical tablets, and 20 mg/mL morphine sulfate oral solutions.

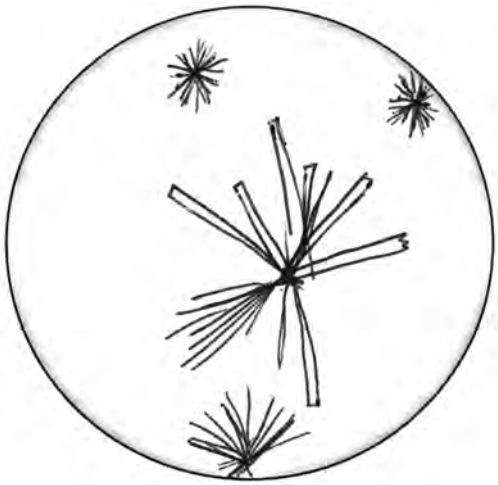
IR Spectrum

See Figure 8. Download SPC file.

PLM Optical Properties

Approximate Size Range	Rosettes: > 50 µm Rosette needles: < 5 µm width, > 50 µm length
Color/Pleochroism	Colorless; 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	Excess liquid was wicked away with filter paper.
Estimated Birefringence	Moderate–High
Extinction	Parallel
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Morphine: Mercuric Chloride (continued)

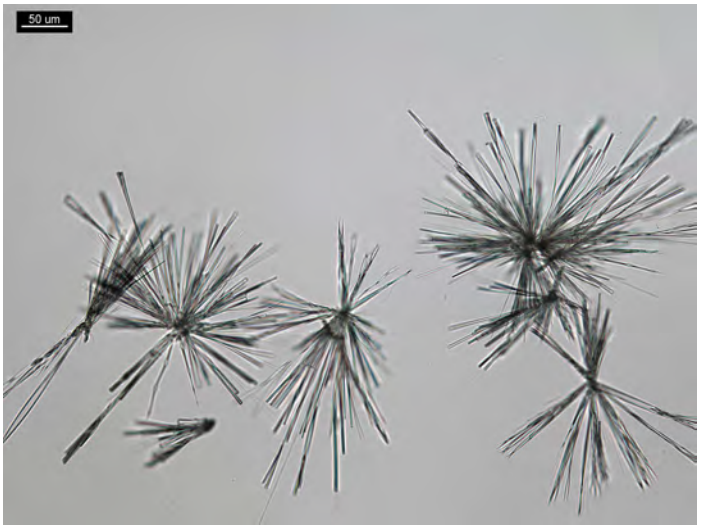

Figure 2. 5 PPP of morphine and 5 µL of $HgCl_2$ reagent form rosettes of needles; no coverslip.

Figure 3. 5 PPP of morphine and 5 µL of $HgCl_2$ reagent form rosettes of needles; with coverslip.

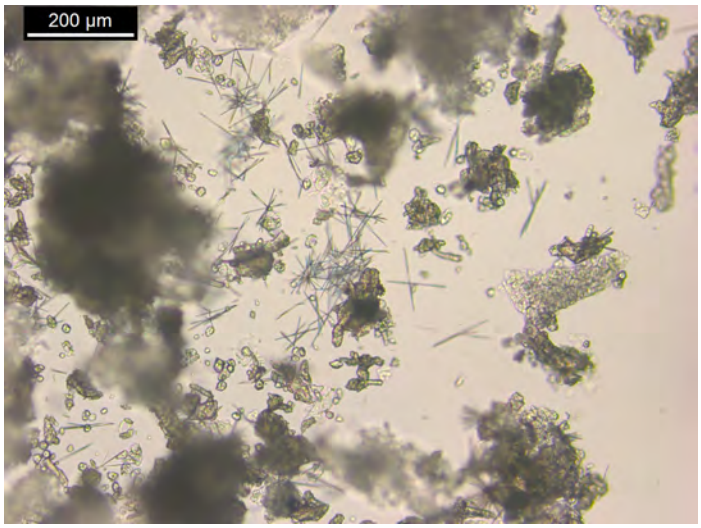

Figure 4. 3 PPP from a 15 mg morphine pharmaceutical tablet and 5 µL of $HgCl_2$ reagent. Crystals form needles and rosettes of needles.

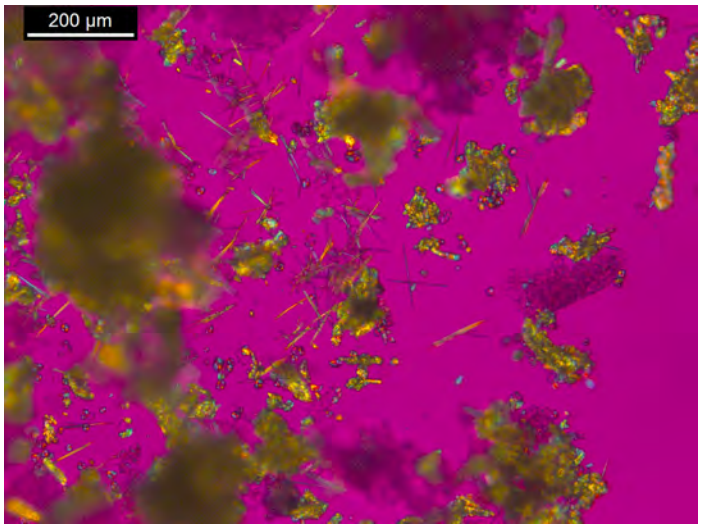

Figure 5. Same as Figure 4. Note negative sign of elongation; crossed polars and Red I compensator.

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Morphine: Mercuric Chloride (continued)

Figure 6. 3 PPP from a 100 mg pharmaceutical tablet and 5 µL of $HgCl_2$ reagent. Crystals form rosettes of needles.

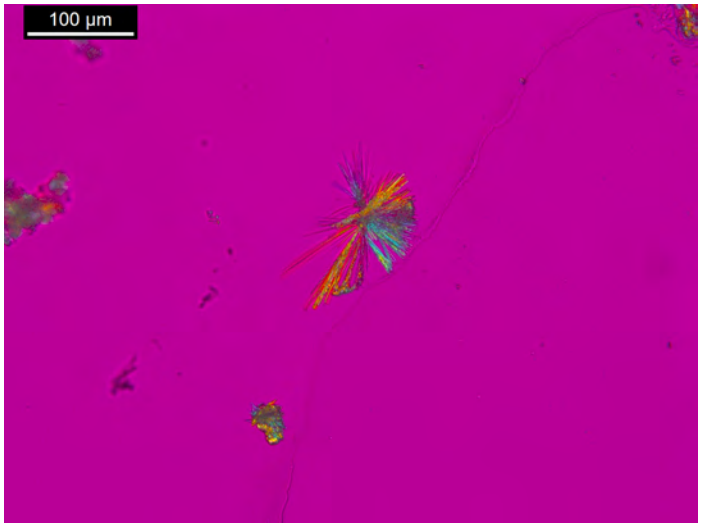

Figure 7. Same as Figure 6. Note negative sign of elongation; crossed polars and Red I compensator.

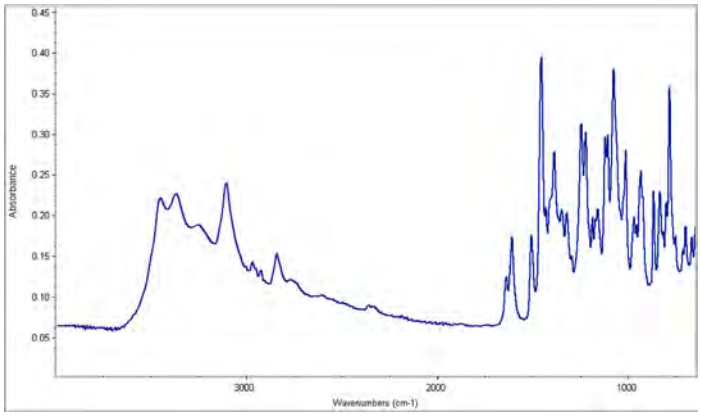

Figure 8. Infrared spectrum of morphine mercuric chloride precipitate. Download SPC file.

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Oxycodone: Platinum Bromide

REAGENT 1: Platinum Bromide (H_2PtBr_6)

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: Place sample on glass slide. Place a 5 µL drop of reagent on a coverslip, invert the coverslip and place it directly onto the sample. Alternatively, dissolve the sample in 5 µL of water on a glass slide. Place a 5 µL drop of reagent on a coverslip, invert the coverslip and place it directly onto the sample. Additional crystallization results when applying back-and-forth pressure to the coverslip with a pencil eraser.

References

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

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈ 4 minutes; ≈ 10–30 seconds when applying back-and-forth pressure to the coverslip

Crystal Morphology and Test Notes

Rosettes of rods and blades, and some smaller rectangles

Photomicrograph of Typical Crystals

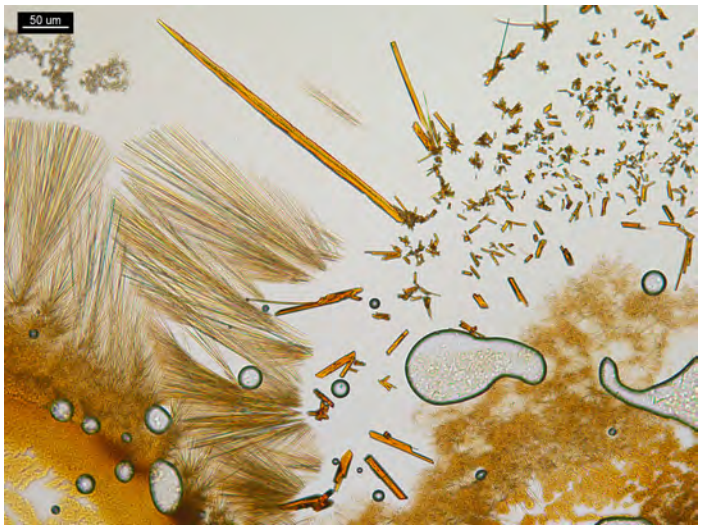


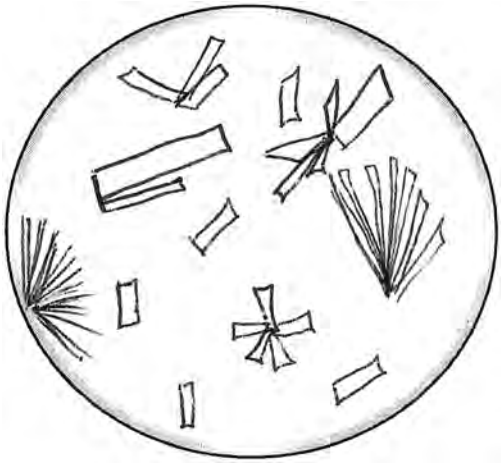
Figure 1. 1 PPP of oxycodone in 5 µL of water and 5 µL of H_2PtBr_6 reagent. Crystals form rods and rosettes.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on a 20 mg oxycodone pharmaceutical tablet using 2 PPP of tablet material; typical crystals grew immediately. This test was also successful on a 20 mg/mL oxycodone oral solution using 5 µL of the solution and 5 µL of reagent; typical crystals grew in ≈ 10 seconds. Pharmaceuticals that contain both acetaminophen and oxycodone required an extraction to separate the oxycodone from acetaminophen that otherwise interferes with the test: A portion of the tablet (≈ 3 mm x 3 mm x 3 mm) was placed in a microcentrifuge tube, 100 µL of ammonium hydroxide were added, then agitated. Then, ≈ 50 µL of chloroform were added, agitated, and the layers were allowed to separate. A 5 µL drop of the chloroform

Continued on following page

PLM Optical Properties

Approximate Size Range	2.5–20 µm width; 15 to > 1 mm length
Color/Pleochroism	Yellow. Pleochroic: yellow to pale yellow
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 filter paper then washed with absolute ethanol and dried at room temperature.
Estimated Birefringence	High. Anomalous first-order gray interference colors appear blue.
Extinction	Parallel; rarely oblique (up to 6°)
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Oxycodone: Platinum Bromide (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

(bottom) layer was placed onto a glass slide using a micropipette. After the drop was allowed to dry, the direct test was performed; typical crystals formed within 10 minutes. This test was also successful on a oxycodone pharmaceutical gel after performing an acetone extraction directly on a glass slide: A small drop of acetone was placed on the gel, then allowed to dry. A 5 µL drop of reagent was placed on a coverslip, inverted and placed directly onto the residue left behind by the dried acetone. Note: Acetaminophen and platinum bromide form rods with a negative sign of elongation.

IR Spectrum

See Figure 13. Download SPC file.

Figure 2. 1 PPP oxycodone in 5 µL of water and 5 µL of H_2PtBr_6 reagent. Crystals form yellow elongated rods.

Figure 3. 1 PPP oxycodone in 5 µL of water and 5 µL of H_2PtBr_6. Crystals form yellow rosettes of elongated rods and needles.

Figure 4. 1 PPP oxycodone in 5 µL of water and 5 µL of H_2PtBr_6 reagent. Crystals form rods and blades.

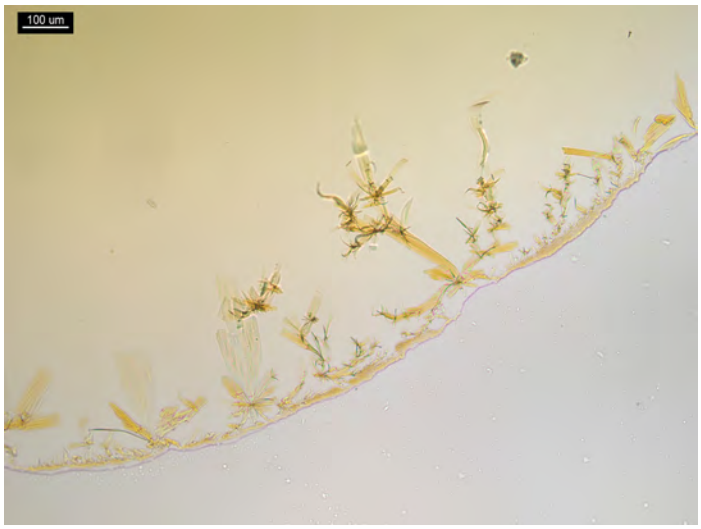

Figure 5. 1 PPP oxycodone in 5 µL of water and 5 µL of H_2PtBr_6 reagent. Crystals form rods and blades.

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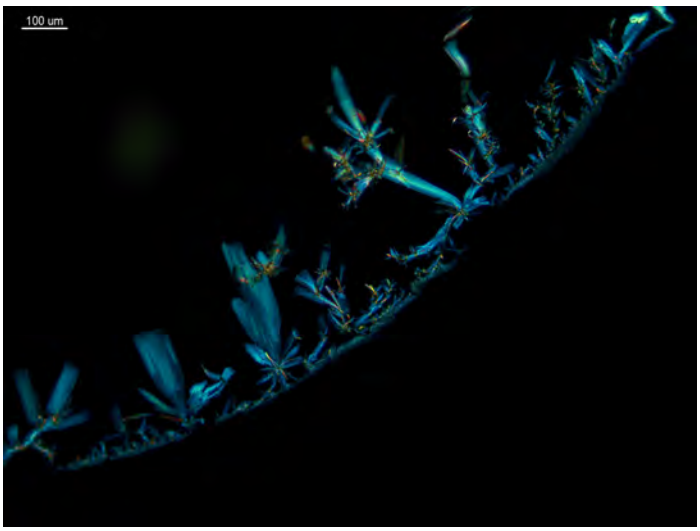

Figure 6. Same as Figure 5. Anomalous first-order gray interference colors appear blue; crossed polars.

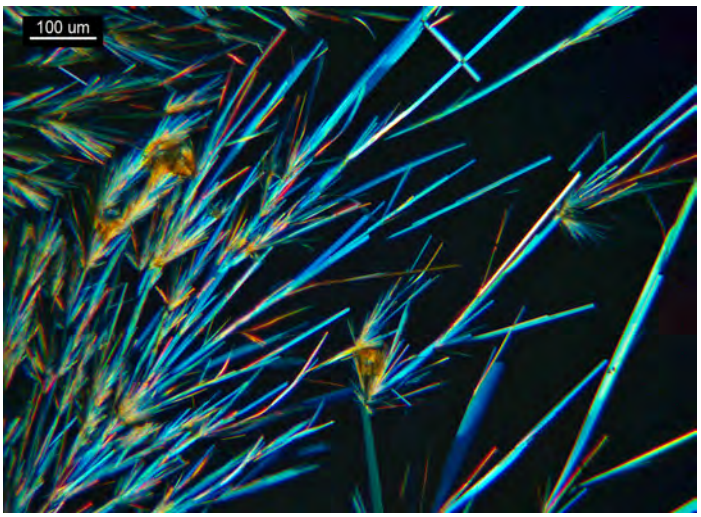

Figure 7. 1 PPP oxycodone in 5 µL of water and 5 µL of H_2PtBr_6 reagent. Anomalous first-order gray interference colors appear blue; crossed polars.

Figure 8. 2.5 µL from a 20 mg/mL oxycodone oral solution in 2.5 µL of water and 5 µL of H_2PtBr_6 reagent. Crystals form rosettes of blades.

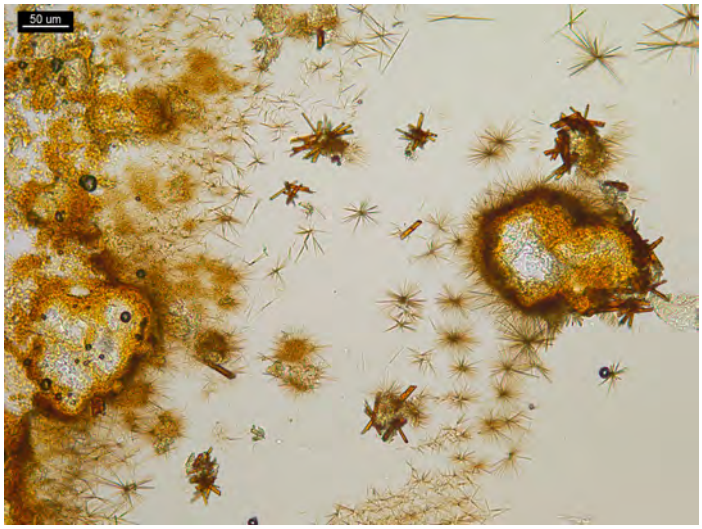

Figure 9. 2 PPP from a 20 mg oxycodone tablet and 5 µL of H_2PtBr_6 reagent. Crystals form rosettes of rods and blades.

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Oxycodone: Platinum Bromide (continued)

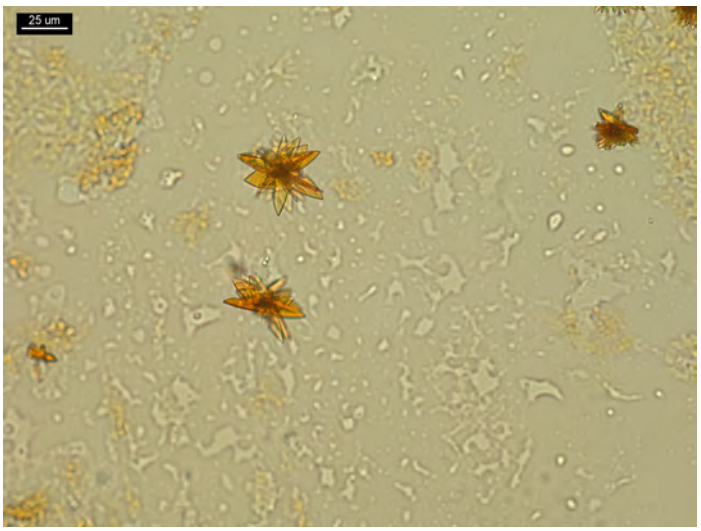

Figure 10. Oxycodone gel and 5 µL of H_2PtBr_6 reagent after acetone extraction. Crystals form rosettes of blades.

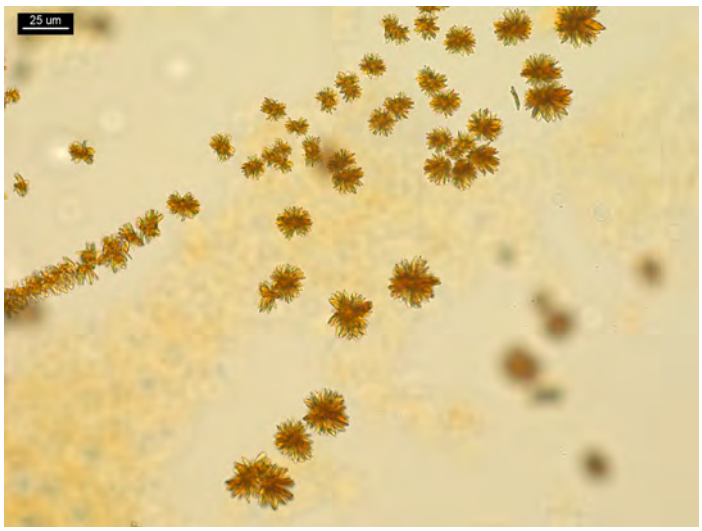

Figure 11. Oxycodone gel and 5 µL of H_2PtBr_6 reagent after acetone extraction. Crystals form rosettes of blades.

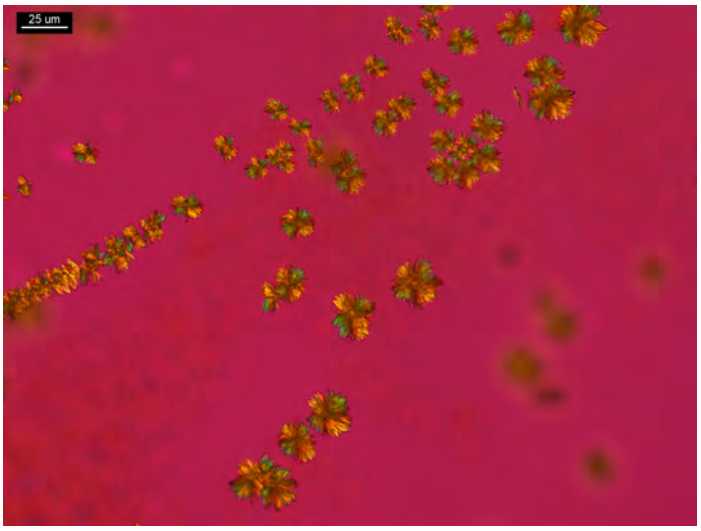

Figure 12. Same as Figure 10; crossed polars and Red I compensator.

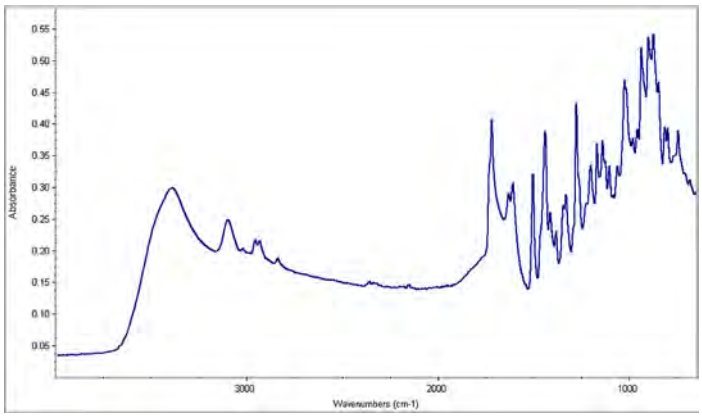

Figure 13. Infrared spectrum of oxycodone platinum bromide precipitate. Download SPC file.

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Oxycodone: Potassium Tri-iodide (Clarke's I-KI, No. 1)

REAGENT 2: Potassium Tri-iodide (Clarke's I-KI, No. 1)

2 g I_2 and 4 g KI in H_2O, make up to 100 mL

Test Method

Direct test: Dissolve the sample in 5 µL of water on a glass slide. Place a 5 µL drop of reagent on a coverslip, invert the coverslip and place it directly onto the sample.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

≈ 1 minute

Crystal Morphology and Test Notes

Numerous small, dark particles replaced by dark red rods, polygonal shapes, plates and prisms.

Photomicrograph of Typical Crystals

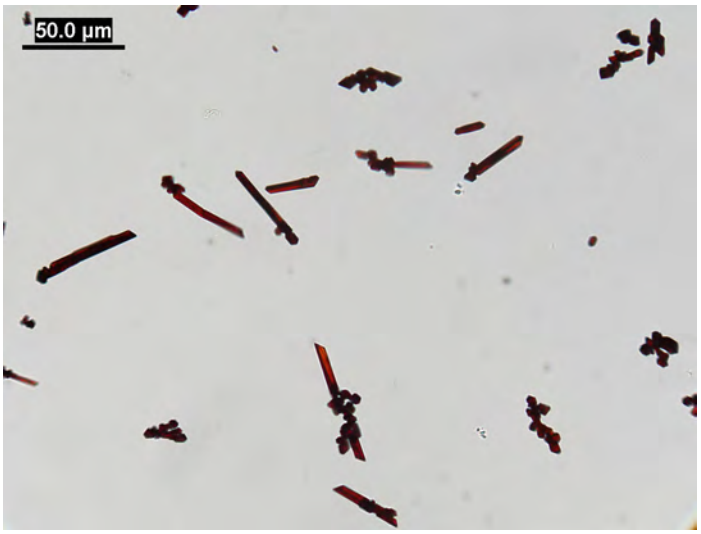

Figure 1. 1 PPP oxycodone in 5 µL of water and 5 µL of potassium tri-iodide reagent. Crystals form dark red rods and plates.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on 5 mg (containing 500 mg acetaminophen) and 20 mg oxycodone pharmaceutical tablets using 2 PPP of tablet material. A 2.5 mg oxycodone tablet (containing 325 mg acetaminophen) required 10 PPP of tablet material and 10 µL of reagent, and an extraction with ammonium hydroxide and chloroform produced the same result. However, typical crystals that formed with the 5 mg and 2.5 mg tablets, with or without extraction, were smaller and polygonal; larger amounts of tablet material produced quicker results. This test was also successful on a 20 mg/mL oxycodone oral solution using 5 µL of the solution and 5 µL of reagent; crystals formed in ≈ 2 minutes. Crystals formed even when diluting 2 µL of solution with 5 µL of water. This test was successful on an oxycodone pharmaceutical gel after an acetone extraction: A small drop of acetone was placed on the gel, then drawn away using a tungsten needle. After the acetone evaporated, a coverslip with a 5 µL drop of reagent was placed onto the dried residue.

PLM Optical Properties

Approximate Size Range	15–50 µm width; 20–150 µm length
Color/Pleochroism	Dark red; not pleochroic
Refractive Indices (RI)	All n > 1.700
Morphology Illustration	*not to scale*
How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature.
Estimated Birefringence	Indeterminable (nearly opaque)
Extinction	Parallel; incomplete
Sign of Elongation	Positive (+); very difficult to determine because of dark color.
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 7. Download SPC file.

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Oxycodone: Potassium Tri-iodide (Clarke's I-KI, No. 1) (continued)

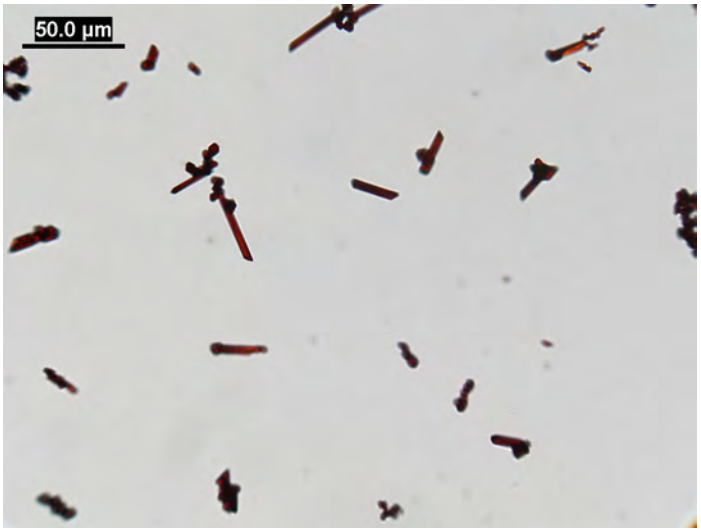

Figure 2. 1 PPP oxycodone in 5 µL of water and 5 µL of potassium tri-iodide reagent. Crystals form dark red rods and prisms.

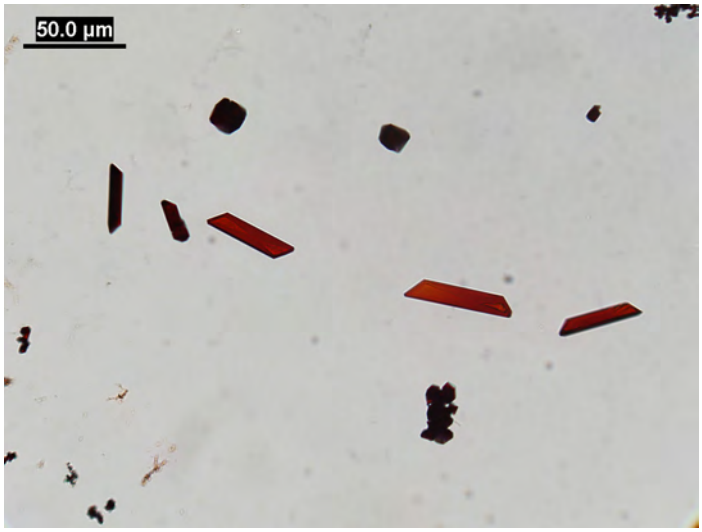

Figure 3. 1 PPP oxycodone in 5 µL of water and 5 µL of potassium tri-iodide reagent. Crystals form dark red rods, prisms and polygonal shapes.

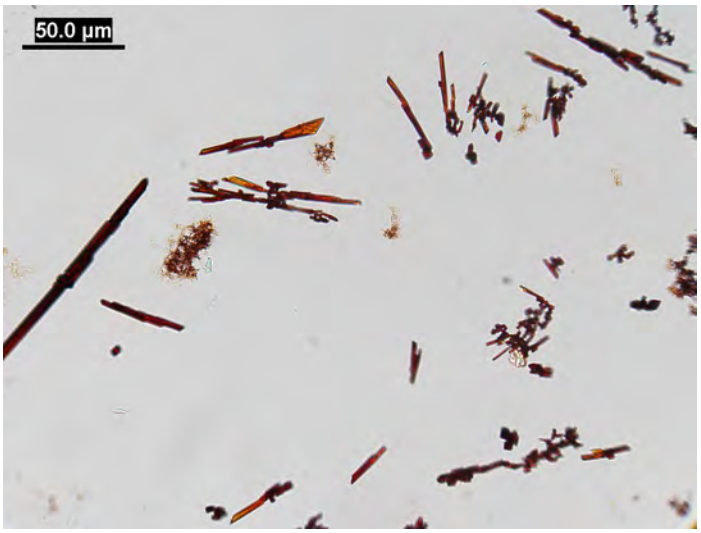

Figure 4. 1 PPP oxycodone in 5 µL of water and 5 µL of potassium tri-iodide reagent. Crystals form dark red, elongated rods and prisms.

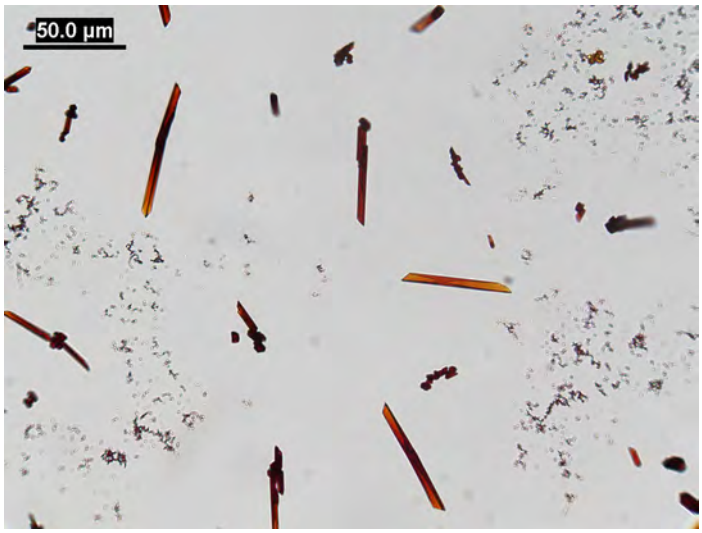

Figure 5. 1 PPP oxycodone in 5 µL of water and 5 µL of potassium tri-iodide reagent. Crystals form dark red, elongated rods and prisms out of numerous small, dark particles.

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Oxycodone: Potassium Tri-iodide (Clarke's I-KI, No. 1) (continued)

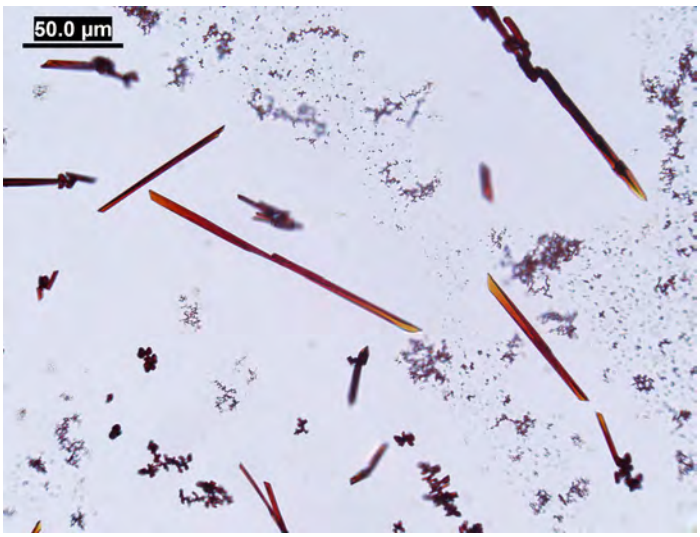

Figure 6. 5 µL from a 20 mg/mL oxycodone oral solution and 5 µL of potassium tri-iodide reagent. Crystals form dark red, elongated rods and prisms.

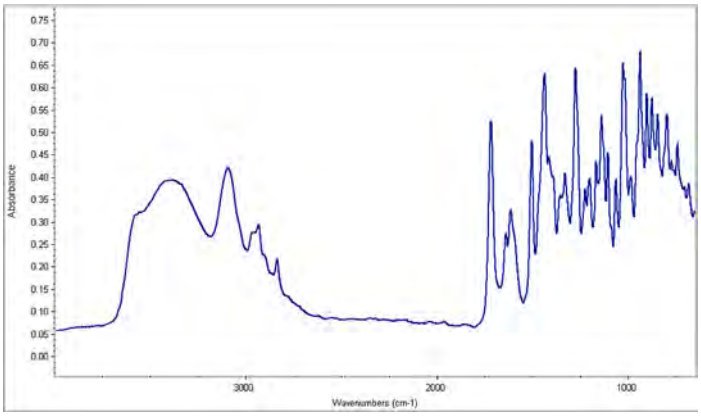

Figure 7. Infrared spectrum of oxycodone potassium tri-iodide precipitate. Download SPC file.

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Oxycodone: Sodium Carbonate

REAGENT 3: Sodium Carbonate (Na_2CO_3)

5% aqueous: 5 g sodium carbonate (Na_2CO_3) in H_2O, make up to 100 mL

Test Method

Direct test: Dissolve the sample in 5 µL of water on a glass slide, then add 5 µL of reagent; no coverslip.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Lightning bolt- and X-shaped crystals, clusters and stars of rods form first at edge of drop; also crystals shaped like pants.

Photomicrograph of Typical Crystals

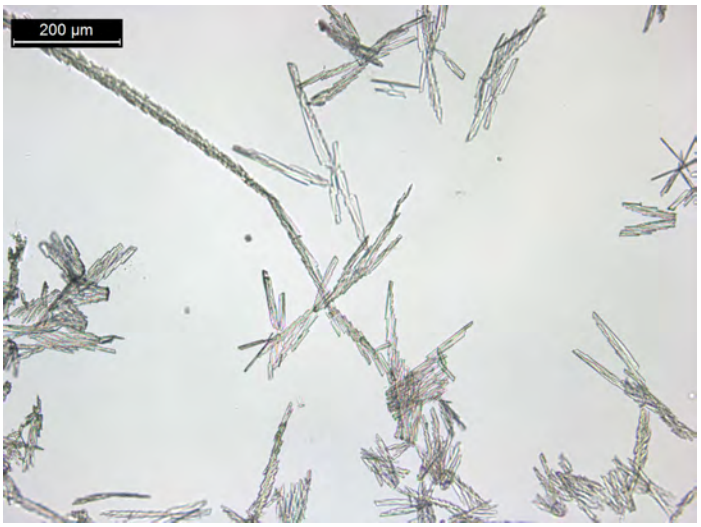

Figure 1. 1 PPP of oxycodone in 5 µL of water and 5 µL of Na_2CO_3 reagent. Crystals form clusters and stars of rods, lightning bolts and X shapes.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on the following oxycodone pharmaceutical tablets: 5 mg (containing 500 mg acetaminophen) using 2 PPP of tablet material and 20 mg using 1 PPP of tablet material. This test was successful on a 2.5 mg oxycodone pharmaceutical tablet (containing 325 mg acetaminophen) only after performing an extraction: A portion of the tablet (≈ 3 mm x 3 mm x 3 mm) was placed in a microcentrifuge tube, 100 µL of ammonium hydroxide were added then agitated. Then, ≈ 50 µL of chloroform were added, agitated, and the layers were allowed to separate. A 5 µL drop of the chloroform (bottom) layer was placed onto a glass slide using a micropipette. After the drop was allowed to dry, the direct test was performed; typical crystals formed within 1 minute. This test was successful on a 20 mg/mL oxycodone oral solution using 5 µL of the solution and 5 µL of reagent. This test was unsuccessful on an oxycodone pharmaceutical gel, and no typical crystals formed.

PLM Optical Properties

Approximate Size Range	5–20 µm width; 50 to > 1 mm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n > 1.500. Crystals are soluble in 1.660 and 1.700 RI liquids.

Morphology Illustration

not to scale

How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature.
Estimated Birefringence	Moderate–High
Extinction	Parallel and oblique (≈ 15°)
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 7. Download SPC file.

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Oxycodone: Sodium Carbonate (continued)

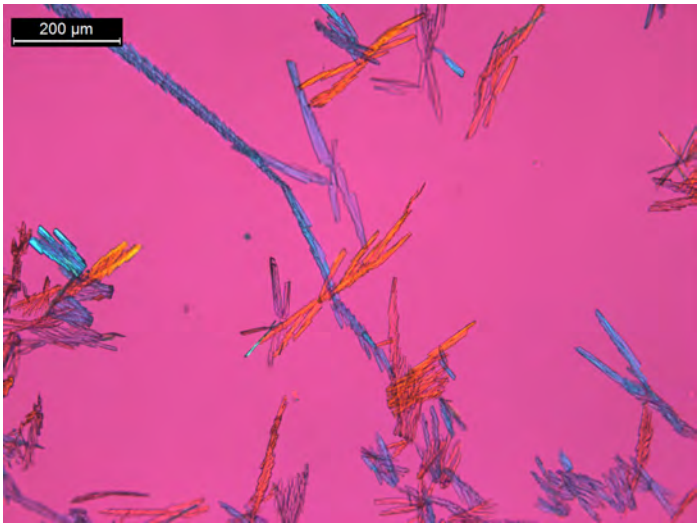

Figure 2. Same as Figure 1; crossed polars and Red I compensator.

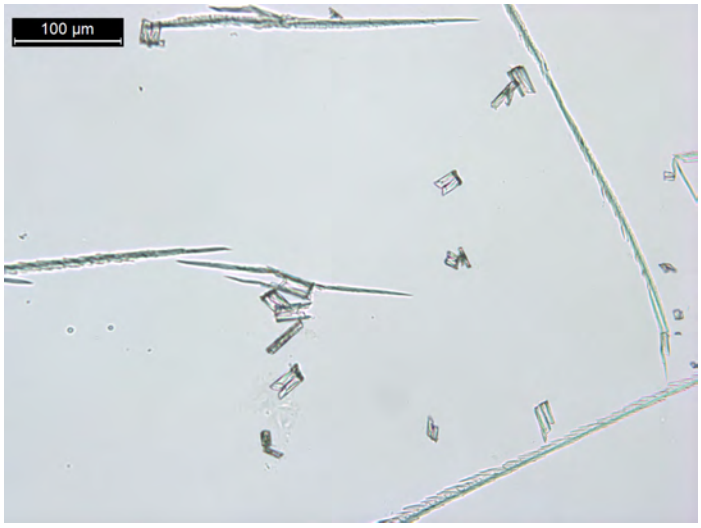

Figure 3. 1 PPP of oxycodone in 5 µL of water and 5 µL of Na_2CO_3 reagent. Crystals form large rods and small pants shapes.

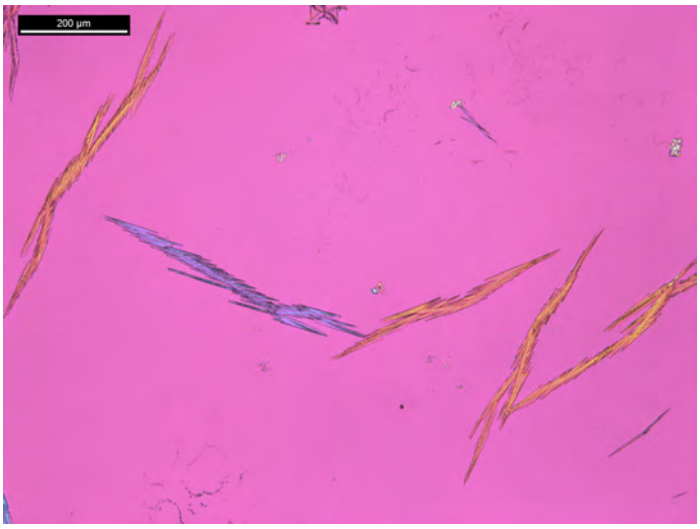

Figure 4. 1 PPP of oxycodone in 5 µL of water and 5 µL of Na_2CO_3 reagent. Crystals form lightning bolts and X shapes; crossed polars and Red I compensator.

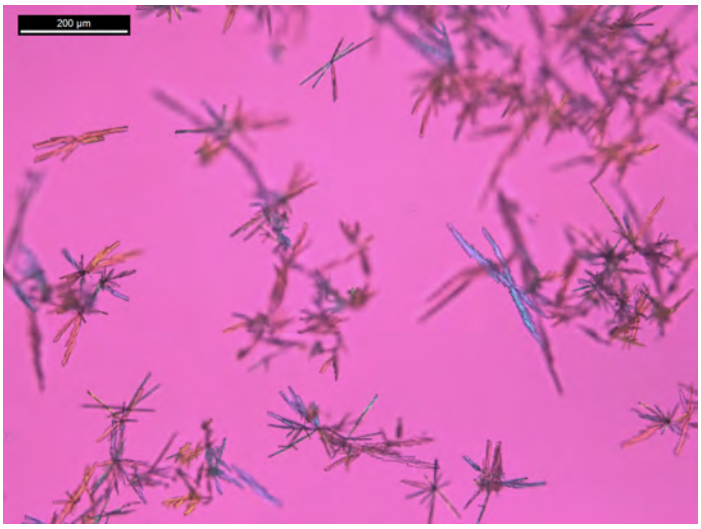

Figure 5. 1 PPP of oxycodone in 5 µL of water and 5 µL of Na_2CO_3 reagent. Crystals form clusters and stars of rods, lightning bolts and X shapes; crossed polars and Red I compensator.

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Oxycodone: Sodium Carbonate (continued)

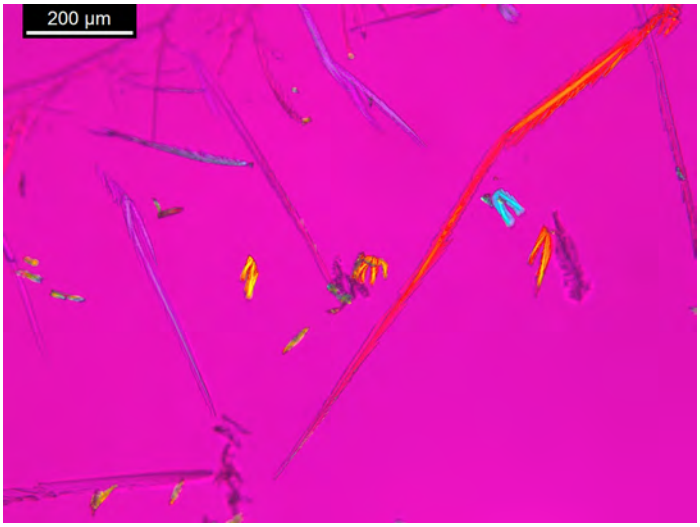

Figure 6. 5 µL from a 20 mg/mL oxycodone oral solution in 5 µL of water and 5 µL of Na_2CO_3 reagent. Crystals form large lightning bolts, X shapes and small pants shapes.

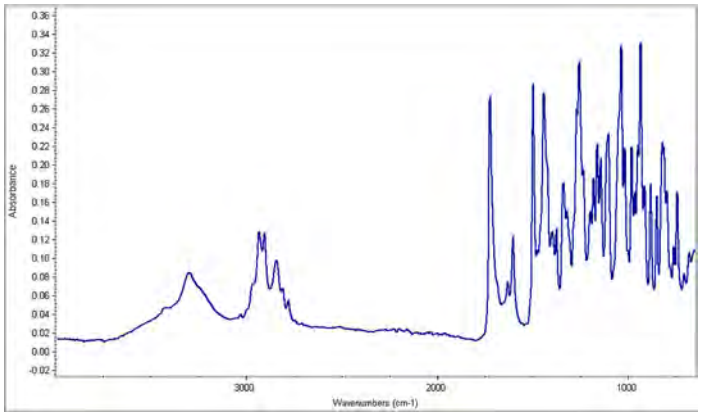

Figure 7. Infrared spectrum of oxycodone sodium carbonate precipitate. Download SPC file.

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Phencyclidine (PCP): Potassium Permanganate

REAGENT 1: Potassium Permanganate ($KMnO_4$)

2 g of $KMnO_4$ and 5 drops of concentrated H_3PO_4 in H_2O, make up to 100 mL. No crystals will form if the reagent is not fresh.

Test Method

Direct test: Dissolve sample in 5 µL of 20% HOAc. 5 µL of $KMnO_4$ reagent is added directly to the test drop; no coverslip.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.

Limit of Detection

1 PPP

Time Required for Crystal Formation

Immediate

Crystal Morphology and Test Notes

Bow ties, butterflies, squares, rectangles and X-shaped crystals. Serrated rods and needles are sometimes visible.

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of PCP in 5 µL of 20% HOAc and 5 µL of $KMnO_4$ reagent. Crystals form bow ties, butterflies, rectangles, rods and X-shaped crystals.

Pharmaceuticals, Adulterants or Other Drug Interactions

Not applicable

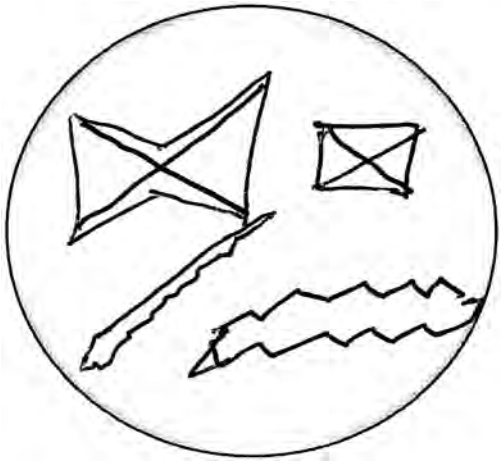
IR Spectrum

See Figure 6. Download SPC file.

PLM Optical Properties

Approximate Size Range	Serrated rods: 5–30 µm width; 10 to > 1 mm length Squares, rectangles and butterflies: 10–100 µm
Color/Pleochroism	Purple; not pleochroic. (After the drop begins to dry, the purple color changes to pale red and the crystals become isotropic.)
Refractive Indices (RI)	n > 1.700. (After addition of RI liquid, the pale red crystals turn light brown and become isotropic.)

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper then dried at room temperature.
Estimated Birefringence	Moderate
Extinction	Parallel and incomplete
Sign of Elongation	Positive (+) and negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Phencyclidine (PCP): Potassium Permanganate (continued)

Figure 2. 1 PPP of PCP in 5 µL of 20% HOAc and 5 µL of $KMnO_4$ reagent. Crystals form bow ties and rectangles.

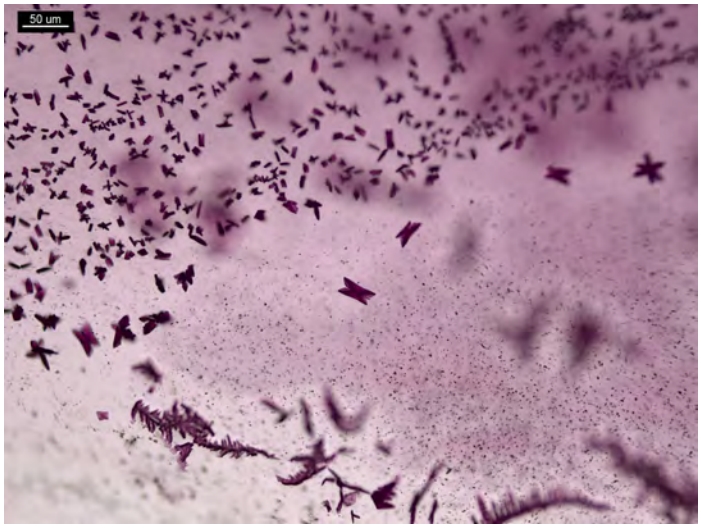

Figure 3. 1 PPP of PCP in 5 µL of 20% HOAc and 5 µL of $KMnO_4$ reagent. Crystals form bow ties, butterflies, rectangles and X shapes.

Figure 4. 1 PPP of PCP in 5 µL of 20% HOAc and 5 µL of $KMnO_4$ reagent. Crystals form bow ties and elongated rods.

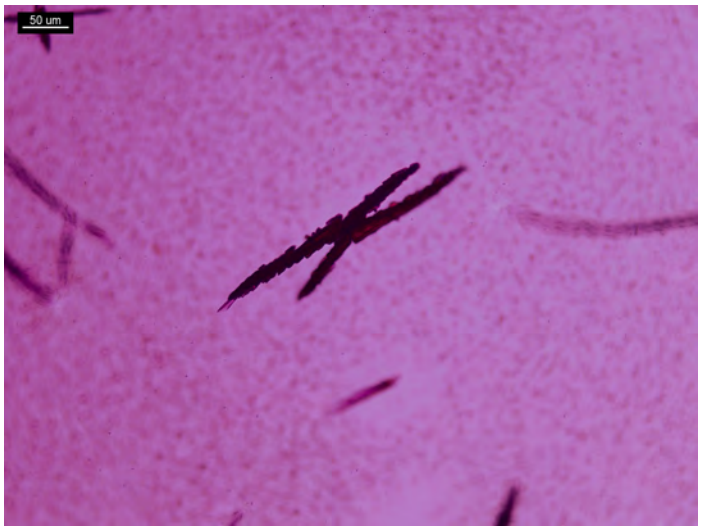

Figure 5. 1 PPP of PCP in 5 µL of 20% HOAc and 5 µL of $KMnO_4$ reagent. Crystals form X shapes; crossed polars and Red I compensator.

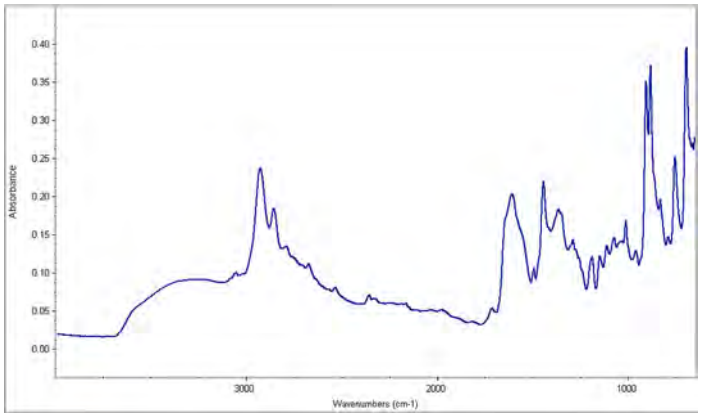

Figure 6. Infrared spectrum of PCP potassium permanganate precipitate. Download SPC file.

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Phencyclidine (PCP): Ammonium Thiocyanate

REAGENT 2: Ammonium Thiocyanate (NH_4SCN)

10% aqueous: 10 g of NH_4SCN in H_2O, make up to 100 mL

Test Method

Direct test: Dissolve sample in 5 µL of 10% HOAc. 5 µL of ammonium thiocyanate reagent is added directly to the test drop. No crystals will form if the reagent is not fresh.

References

1. Alvarez, J. "Part 1: Analytical Data on the Thiophene Analog of Phencyclidine," *Microgram*, 10:9, pp 120–131, September 1977.

Limit of Detection

2 PPP

Time Required for Crystal Formation

Immediately

Crystal Morphology and Test Notes

Rods, blades and rosettes of blades

Photomicrograph of Typical Crystals

Figure 1. 2 PPP of sample dissolved in 5 µL of 20% HOAc and 5 µL of NH_4SCN reagent. Crystals form blades and rosettes of blades.

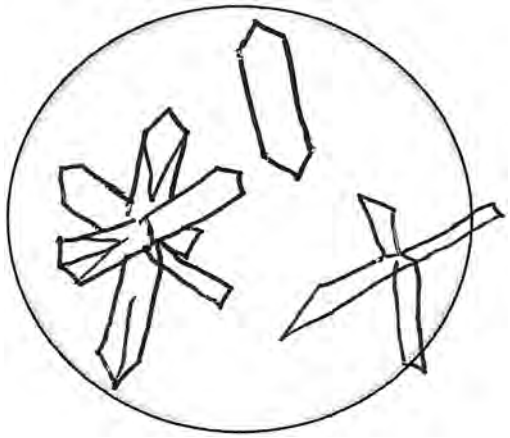
Pharmaceuticals, Adulterants or Other Drug Interactions

Not applicable

IR Spectrum

See Figure 8. Download SPC file.

PLM Optical Properties

Approximate Size Range	5–30 µm width; 50 to > 500 µm length
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	Parallel: ≈ 1.634 Perpendicular: ≈ 1.660
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Excess liquid was wicked away with filter paper, washed with water using a tungsten needle and dried at room temperature.
Estimated Birefringence	Moderate
Extinction	Parallel
Sign of Elongation	Mostly negative (–) and some positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Biaxial (optic sign indeterminable)

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Phencyclidine (PCP): Ammonium Thiocyanate (continued)

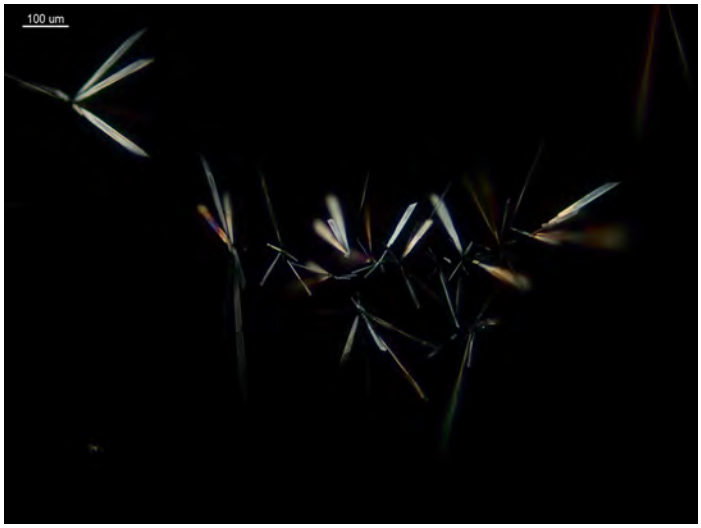

Figure 2. Same as Figure 1; crossed polars.

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

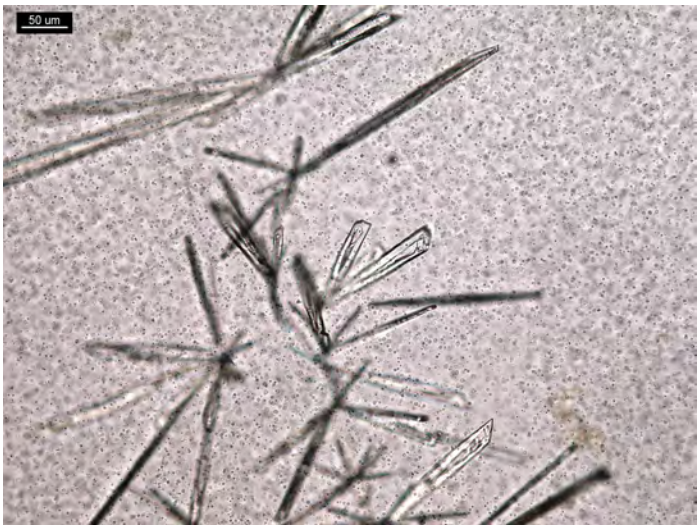

Figure 4. 1 PPP of sample dissolved in 5 µL of 20% HOAc and 5 µL of NH_4SCN reagent. Crystals form blades and rosettes of blades.

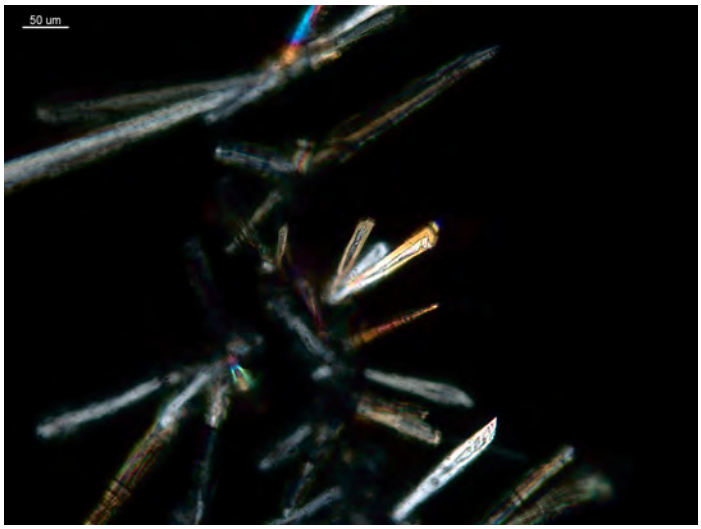

Figure 5. Same as Figure 4; crossed polars.

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Phencyclidine (PCP): Ammonium Thiocyanate (continued)

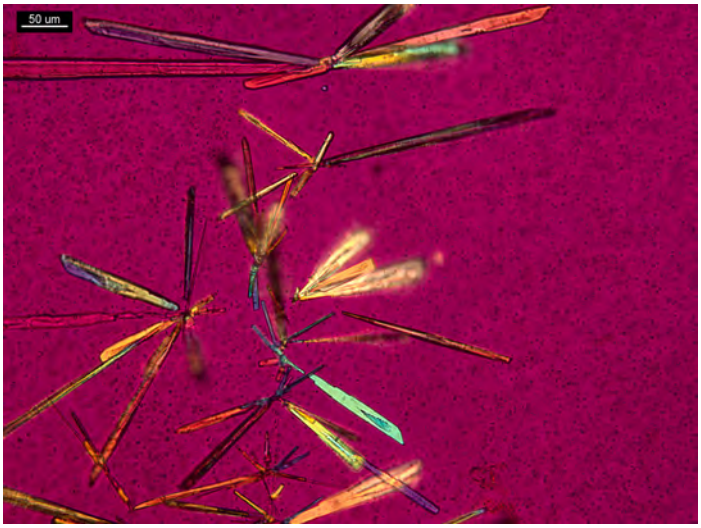

Figure 6. Same as Figure 4; crossed polars and Red I compensator.

Figure 7. 1 PPP of sample dissolved in 5 µL of 20% HOAc and 5 µL of NH_4SCN reagent. Crystals form rosettes of blades; crossed polars and Red I compensator.

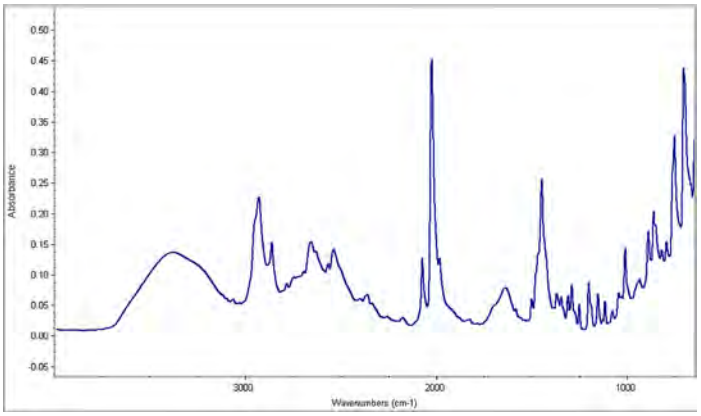

Figure 8. Infrared spectrum of PCP ammonium thiocyanate precipitate. Download SPC file.

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Pseudoephedrine: Dilituric Acid

REAGENT 1: Dilituric Acid (5-Nitrobarbituric Acid)

10 mg dilituric acid in H_2O, make up to 1 mL

Test Method

Direct test: Add 5–10 µL of reagent directly to sample on a glass slide.

References

1. Julian, E.A. and Plein, E.M. "Microcrystalline Identification of Drugs of Abuse: The 'White Cross Suite,'" *Journal of Forensic Sciences*, 26:2, pp 358–367, 1981.

Limit of Detection

1 PPP

Time Required for Crystal Formation

< 1 minute

Crystal Morphology and Test Notes

Six-sided plates and tablets, often distorted and usually elongated, some shaped like coffins. Note: Dilituric acid recrystallizes alone and also forms microcrystals with a variety of substances. Therefore, it is important to confirm refractive indices and sign of elongation. Dilituric acid crystals are smaller and cigar-shaped, and often form together with typical pseudoephedrine crystals. However, dilituric acid crystals have an n-parallel < 1.520, an n-perpendicular > 1.638 and a negative sign of elongation (Figures 6 and 7). High concentrations of pseudoephedrine result in the formation of fewer dilituric acid crystals. Note: *l*-Ephedrine also forms crystals with dilituric acid, but they have a different morphology (parallelograms) different refractive indices (n_1 = 1.544 and n_2 = 1.654) and a negative sign of elongation (Figures 13–15).

Photomicrograph of Typical Crystals

Figure 1. 1 PPP of pseudoephedrine and dilituric acid reagent. Six-sided plates and tablets grow at the edge of the drop within 1 minute.

Pharmaceuticals, Adulterants or Other Drug Interactions

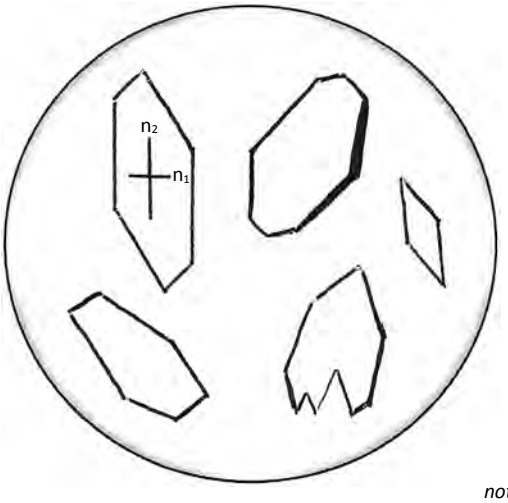
This test was successful on the following pharmaceutical tablets (especially when colorless particles were picked out and tested):

Continued on following page

PLM Optical Properties

Approximate Size Range	50 to > 300 µm
Color/Pleochroism	Colorless; not pleochroic
Refractive Indices (RI)	n_1 = 1.520 n_2 = 1.638

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Positive (+)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable (flash figure)

IR Spectrum

See Figure 16. Download SPC file.

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Pseudoephedrine: Dilituric Acid (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

- Mucus Relief D tablet (40 mg pseudoephedrine HCl and 400 mg guaifenesin)
- Pseudoephedrine generic tablet (30 mg pseudoephedrine HCl)
- Sudafed® 12-hour tablet (120 mg pseudoephedrine HCl and 220 mg naproxen sodium)
- Wal-Phed® tablet (60 mg pseudoephedrine HCl and 4 mg chlorpheniramine maleate)

This test was successful with a children's pseudoephedrine chewable tablet (15 mg pseudoephedrine) after a chloroform extraction: A small portion of tablet material was crushed, placed in a microcentrifuge tube, and 15 µL of chloroform was added and agitated. Then, 10 µL were extracted with a micropipette and dropped onto a glass slide. After the chloroform evaporated, the direct test was performed.

This test was unsuccessful with the following pharmaceuticals using the direct test method or various extraction methods, including acid-base, 70% methanol or chloroform:

- Advil® Allergy Sinus tablet (30 mg pseudoephedrine HCl and 200 mg ibuprofen and 2 mg chlorpheniramine maleate)
- Advil® Cold & Sinus Liqui-Gels (30 mg pseudoephedrine HCl and 200 mg ibuprofen)
- Wal-itin® D Extended Release tablet (240 mg pseudoephedrine sulfate and 10 mg loratadine)
- Wal-Zyr™ D Extended Release tablet (120 mg pseudoephedrine HCl and 5 mg cetirizine HCl)

The failure of the extractions was a result of the extraction liquid immediately becoming viscous and gelatinous after it was added to the tablet portion.

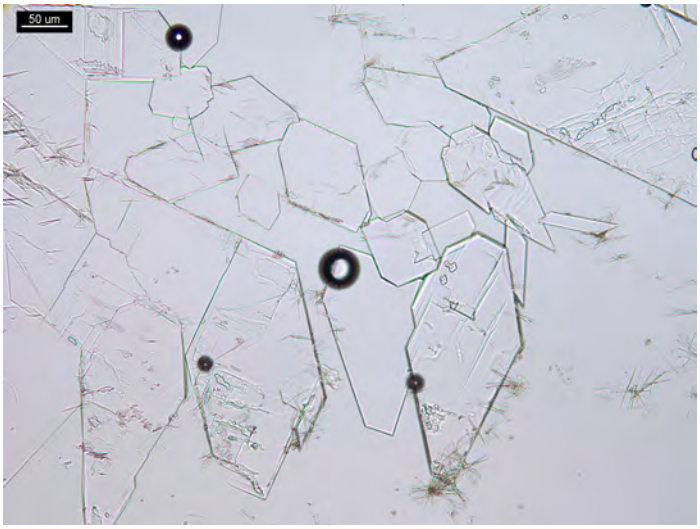

Figure 2. 1 PPP of pseudoephedrine and dilituric acid reagent. Six-sided plates and tablets form at the edge of the drop after 1 minute; dried at room temperature and mounted in 1.660 RI liquid.

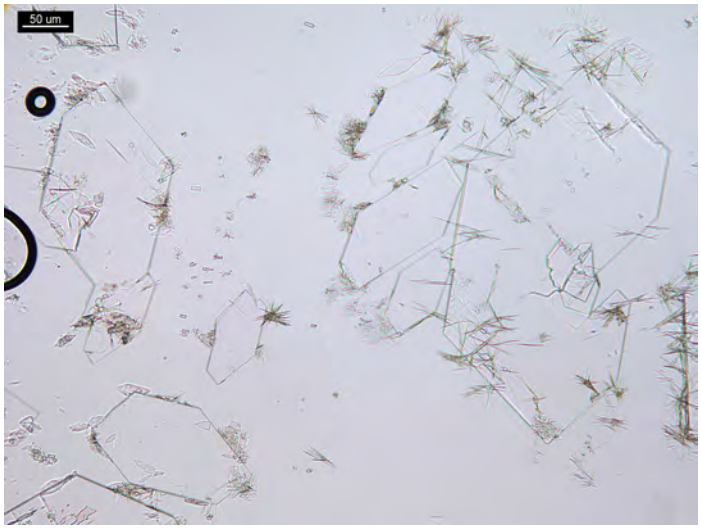

Figure 3. 1 PPP of pseudoephedrine and dilituric acid reagent. Six-sided plates and tablets form at the edge of the drop after 1 minute; dried at room temperature and mounted in 1.660 RI liquid.

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Pseudoephedrine: Dilituric Acid (continued)

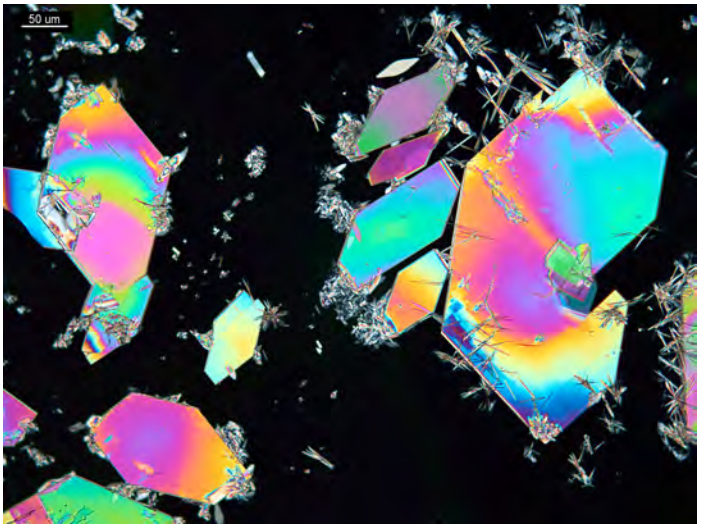

Figure 4. Same as Figure 3; crossed polars.

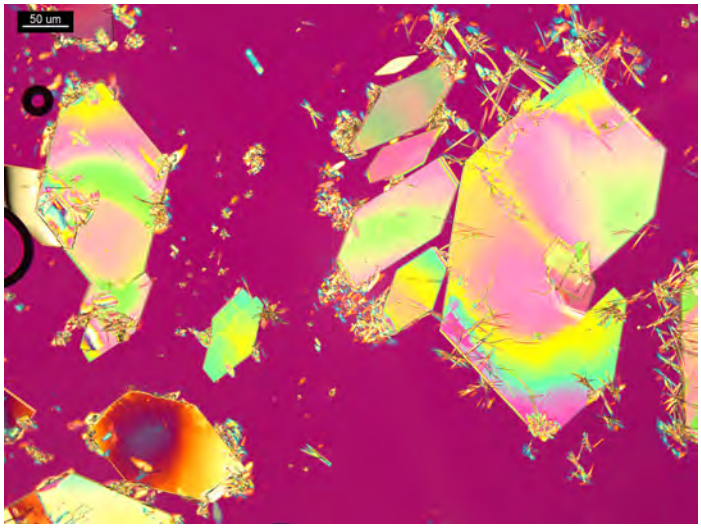

Figure 5. Same as Figure 3. Six-sided plates and tablets have a positive sign of elongation; crossed polars and Red I compensator.

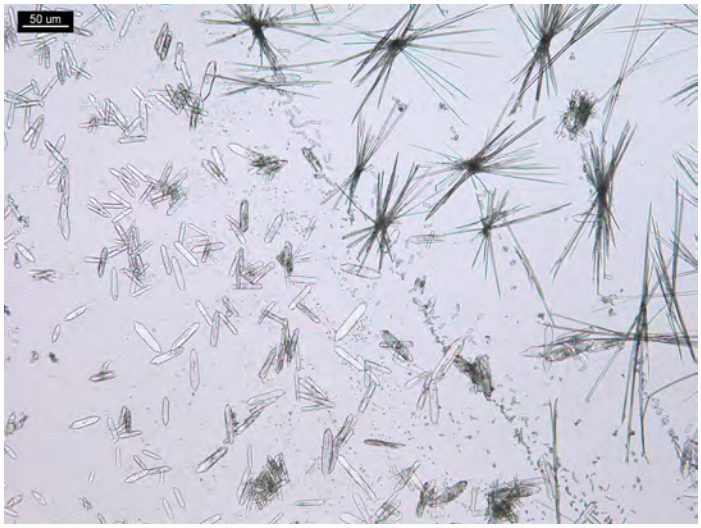

Figure 6. Dilituric acid reagent only (no pseudoephedrine). Small, elongated, cigar-shaped crystals may form (lower left); not to be confused with pseudoephedrine-dilituric acid crystals.

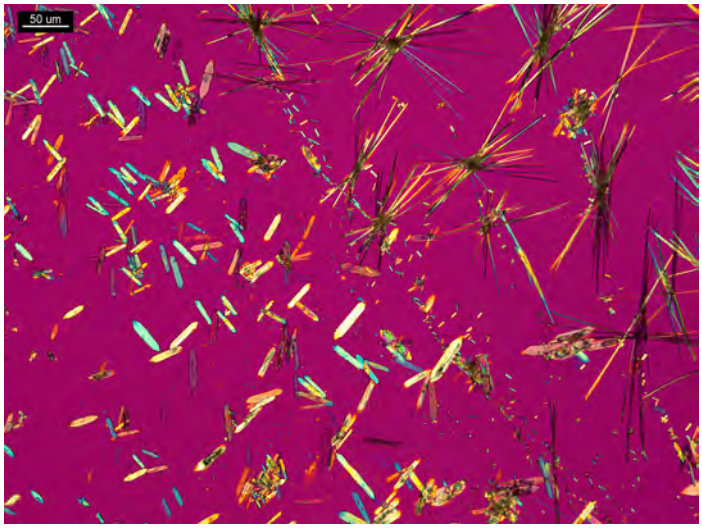

Figure 7. Same as Figure 6. Small, elongated, cigar-shaped crystals have a negative sign of elongation; crossed polars and Red I compensator.

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Pseudoephedrine: Dilituric Acid (continued)

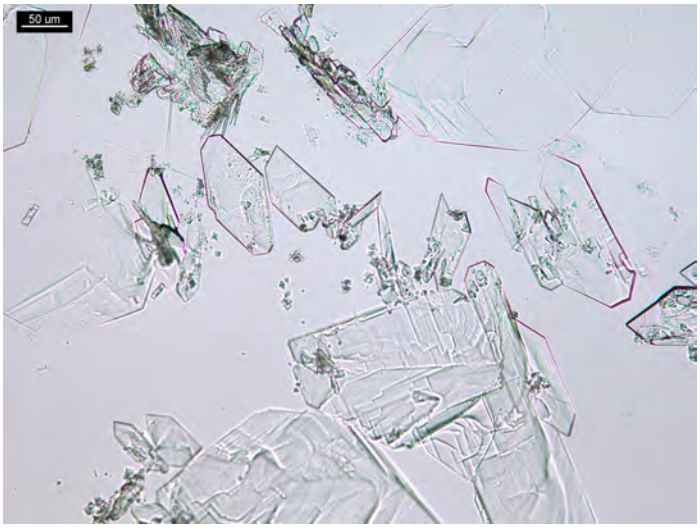

Figure 8. 2 PPP from a Wal-Phed® pharmaceutical tablet (60 mg pseudoephedrine HCl and 4 mg chlorpheniramine maleate) and dilituric acid reagent. Crystals form six-sided plates and tablets.

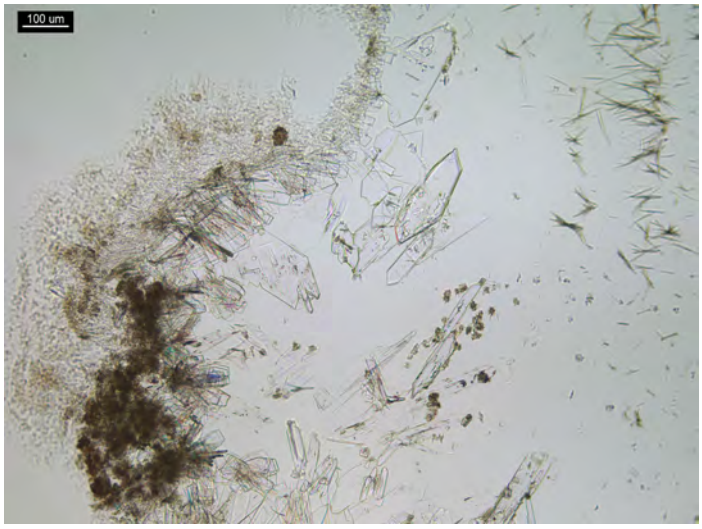

Figure 9. 1 PPP from a Sudafed® 12-hour pharmaceutical tablet (120 mg pseudoephedrine HCl and 220 mg naproxen sodium) and dilituric acid reagent. Crystals form six-sided plates and tablets.

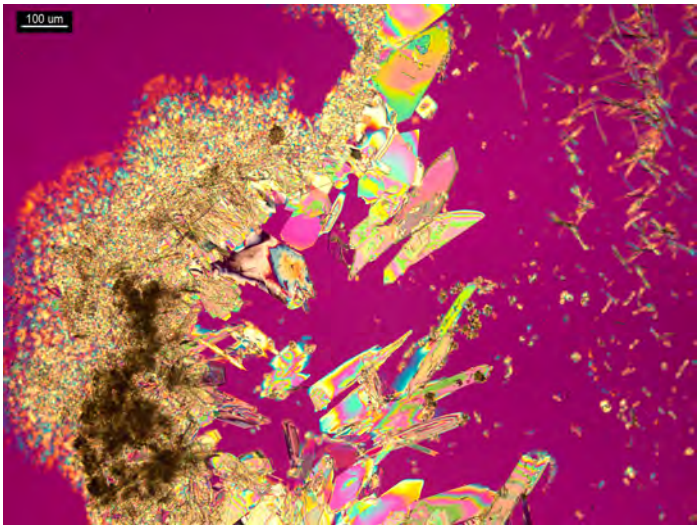

Figure 10. Same as Figure 9: crossed polars and Red I compensator.

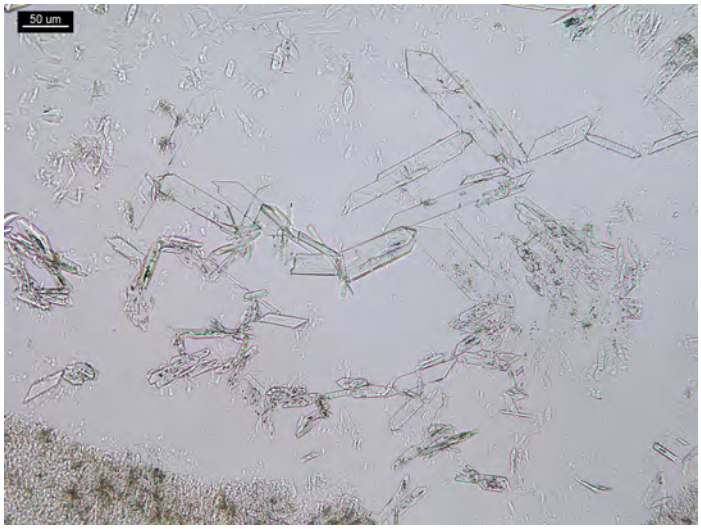

Figure 11. Sudafed® 12-hour pharmaceutical tablet (120 mg pseudoephedrine HCl and 220 mg naproxen sodium) and dilituric acid reagent after acid-base extraction. Crystals form elongated, six-sided tablets and plates.

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Pseudoephedrine: Dilituric Acid (continued)

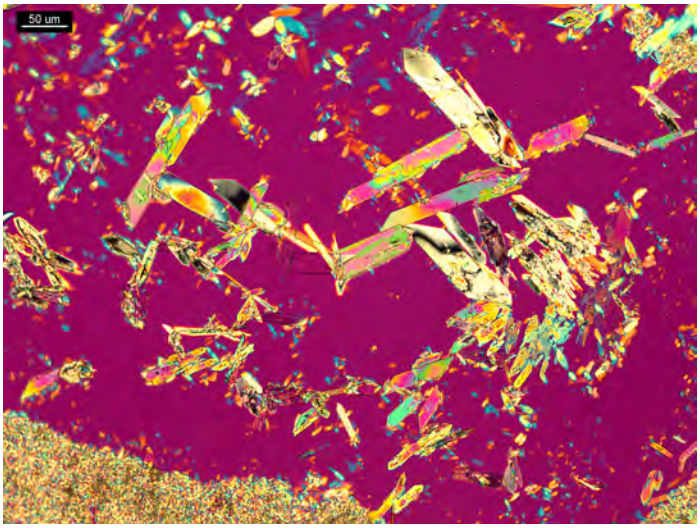

Figure 12. Same as Figure 11; crossed polars and Red I compensator.

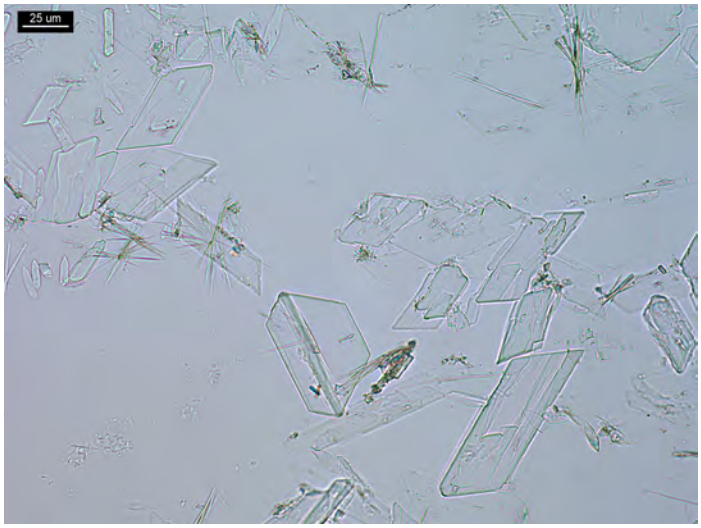

Figure 13. 1 PPP of *l*-ephedrine and dilituric acid reagent. Note different morphology (parallelograms) and different refractive indices (n_1 = 1.544 and n_2 = 1.654).

Figure 14. Same as Figure 13; crossed polars.

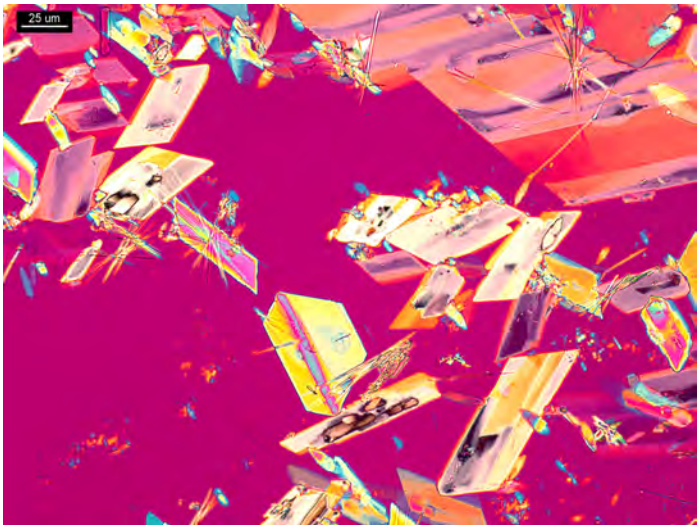

Figure 15. Same as Figure 13. *l*-Ephedrine and dilituric acid reagent crystals (parallelograms) have a negative sign of elongation; crossed polars and Red I compensator.

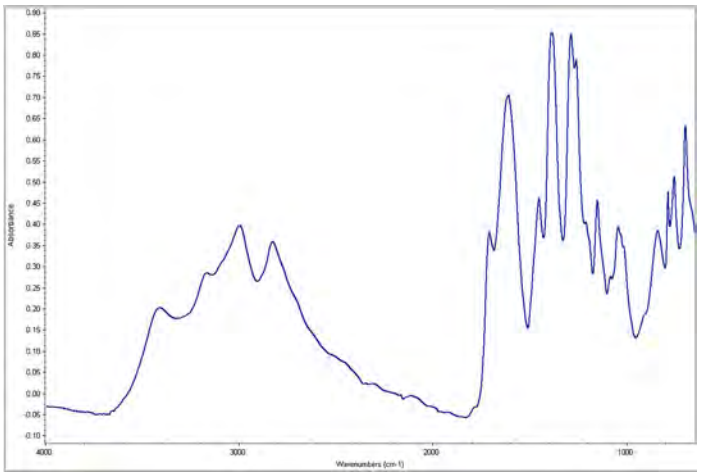

Figure 16. Infrared spectrum of pseudoephedrine dilituric acid precipitate. Download SPC file.

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Pseudoephedrine: Gold Chloride

REAGENT 2: Gold Chloride ($HAuCl_4$)

1 g $HAuCl_4 \cdot 3H_2O$ in (1+2) H_3PO_4, make up to 20 mL. (1+2) H_3PO_4 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

Add 5–10 µL of reagent directly to sample on a glass slide. Note: The concentration of pseudoephedrine affects the test. More than 1 PPP of pseudoephedrine in less than 5 µL of reagent produces immiscible oily drops but no typical crystals.

References

1. Fulton, C. *Modern Microcrystal Tests for Drugs,* Wiley-Interscience: New York, 1969.
2. AOAC Official Methods, 13th Edition, William Horwitz, Ed., Association of Analytical Chemists: Washington, D.C., 1980.

Limit of Detection

1 PPP (> 1 PPP of pseudoephedrine and < 5 µL of reagent produce immiscible oily drops and no typical crystals).

Time Required for Crystal Formation

10–90 minutes

Crystal Morphology and Test Notes

Thin, branching dendrites and combs. Immiscible, yellow oily drops precede crystal formation and migrate to the edge of the reagent drop.

Photomicrograph of Typical Crystals

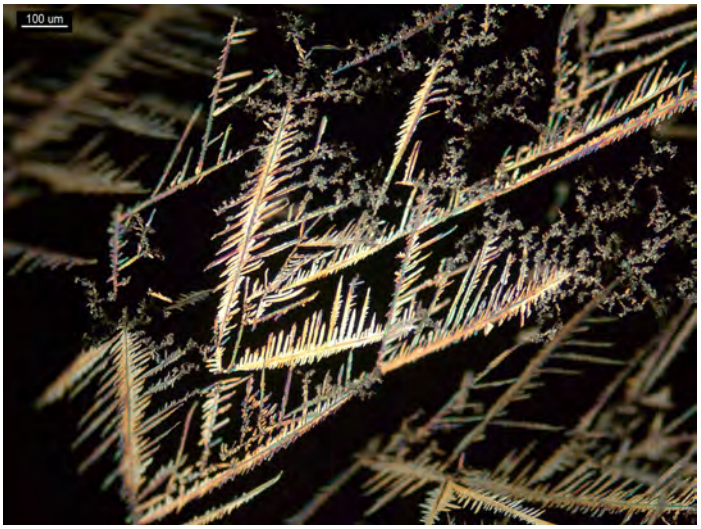


Figure 1. 1 PPP of pseudoephedrine and 5 µL of $HAuCl_4$ reagent. Crystal form thin, branching dendrites and combs; crossed polars.

Pharmaceuticals, Adulterants or Other Drug Interactions

This test was successful on the following pharmaceutical tablets (especially when colorless particles were picked out and tested) Up to 5 PPP of material may be necessary for some pharmaceuticals:

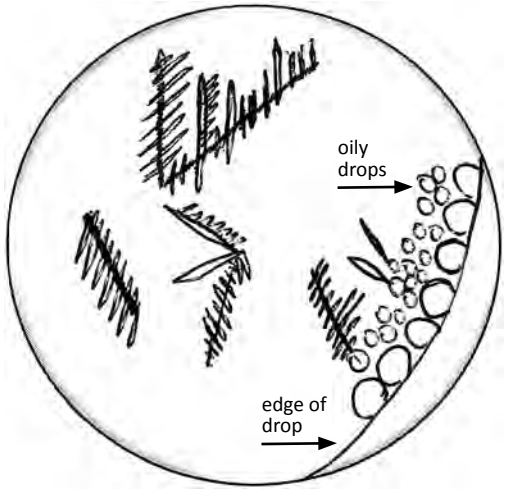
- Advil® Allergy Sinus tablet (30 mg pseudoephedrine HCl and 200 mg ibuprofen and 2 mg chlorpheniramine maleate)
- Mucus Relief-D tablet (40 mg pseudoephedrine HCl and 400 mg guaifenesin)
- Pseudoephedrine generic tablet (30 mg pseudoephedrine HCl)

Continued on following page

PLM Optical Properties

Approximate Size Range	< 5 µm width; 50 to > 500 µm length
Color/Pleochroism	Nearly colorless or pale yellow; not pleochroic
Refractive Indices (RI)	Indeterminable. Crystals are fragile, and excess liquid could not be removed.

Morphology Illustration



not to scale

How Crystals Were Dried for RI Measurement	Crystals are fragile and excess liquid could not be removed.
Estimated Birefringence	High
Extinction	Symmetrical (vibration directions bisect the prominent crystal angle between crystal branches)
Sign of Elongation	Negative (–) for individual crystal branches
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

IR Spectrum

See Figure 11. Download SPC file.

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Pseudoephedrine: Gold Chloride (continued)

Pharmaceuticals, Adulterants or Other Drug Interactions

Continued from preceding page

- Sudafed® 12-hour tablet (120 mg pseudoephedrine and 220 mg naproxen sodium)
- Wal-itin® D Extended Release tablet (240 mg pseudoephedrine sulfate and 10 mg loratadine)
- Wal-Phed® tablet (60 mg pseudoephedrine HCl and 4 mg chlorpheniramine maleate)
- Wal-Zyr™ D Extended Release tablet (120 mg pseudoephedrine HCl and 5 mg cetirizine HCl)

This test was successful with a children's pseudoephedrine chewable tablet (15 mg pseudoephedrine) after a chloroform extraction (Figure 9): A small portion of tablet material was crushed, placed in a microcentrifuge tube, and 15 µL of chloroform was agitated. Then, 10 µL were extracted with a micropipette and dropped onto a glass slide. After the chloroform evaporated, the direct test was performed.

This test was unsuccessful with the following pharmaceutical using the direct test method, or acid-base extraction, 70% methanol extraction or chloroform extraction:
Advil® Cold & Sinus Liqui-Gels (30 mg pseudoephedrine HCl and 200 mg ibuprofen)

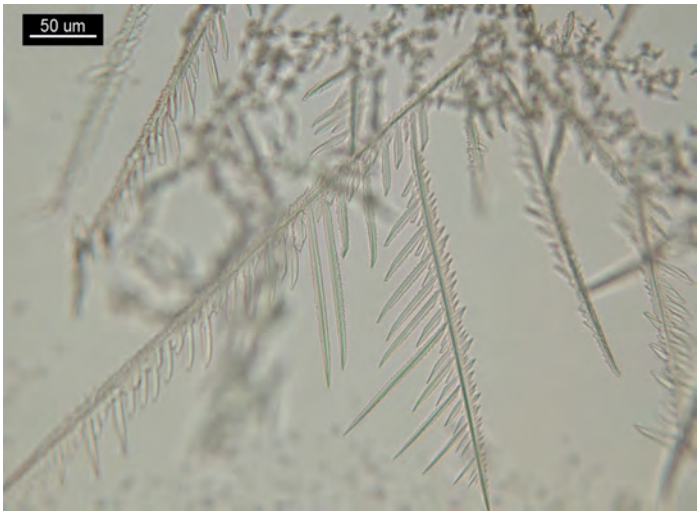

Figure 2. 1 PPP from a Wal-Zyr™ D pharmaceutical tablet (120 mg pseudoephedrine HCl and 5 mg cetirizine HCl) and 5 µL of $HAuCl_4$ reagent. Crystals form thin branches and combs.

Figure 3. Same as Figure 2; crossed polars.

Figure 4. Same as Figure 2; crossed polars and Red I compensator.

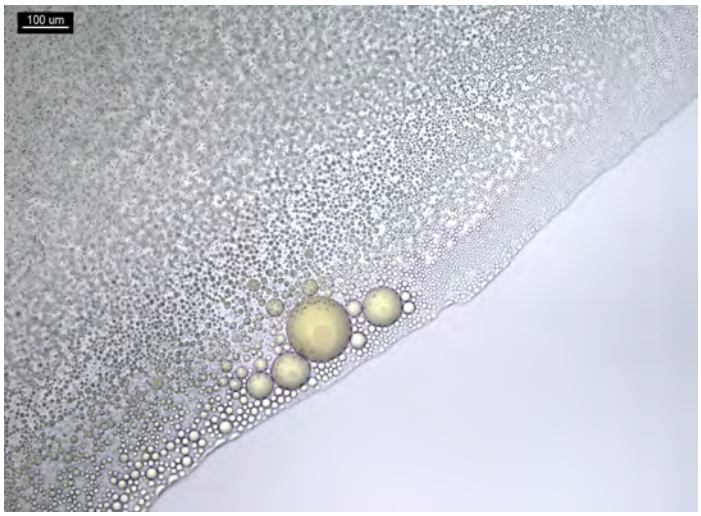

Figure 5. 1 PPP of pseudoephedrine and 5 µL of $HAuCl_4$ reagent. Immiscible, yellow oily drops that precede crystal formation migrate to the edge of the reagent drop.

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Pseudoephedrine: Gold Chloride (continued)

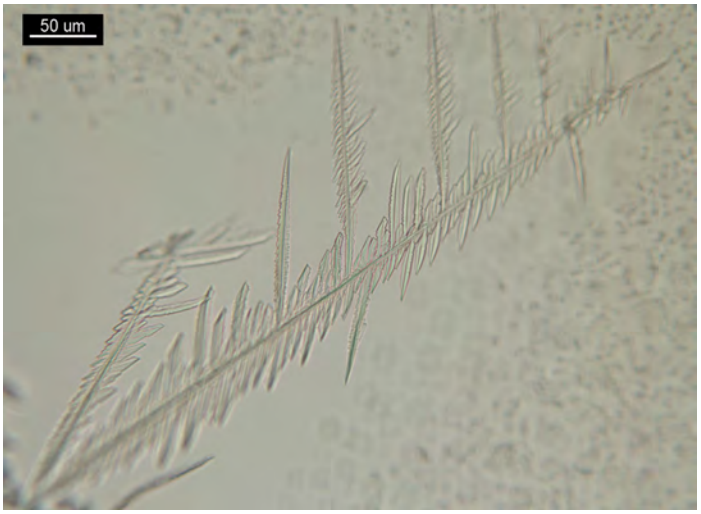

Figure 6. 1 PPP of Sudafed® 12-Hour pharmaceutical tablet (120 mg pseudoephedrine and 220 mg naproxen sodium) and 5 µL of $HAuCl_4$ reagent. Crystals form branches and combs.

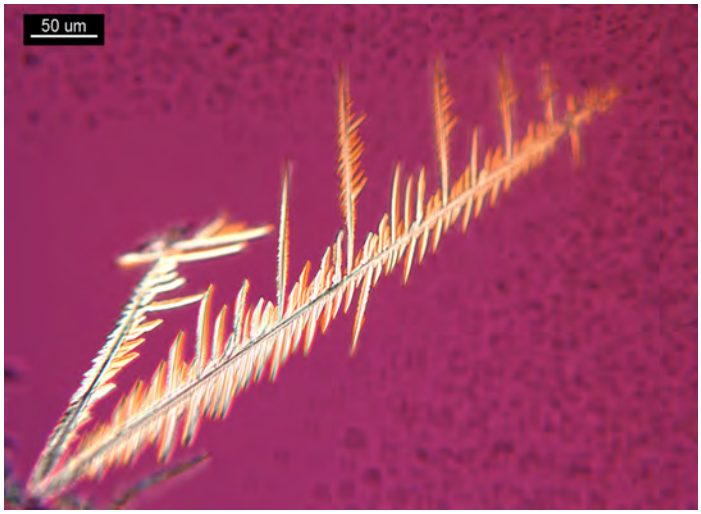

Figure 7. Same as Figure 6. Thin, branching dendrites have a negative sign of elongation; crossed polars and Red I compensator.

Figure 8. 1 PPP of Wal-itin® D pharmaceutical tablet (240 mg pseudoephedrine sulfate and 10 mg loratadine) and 5 µL of $HAuCl_4$ reagent. Crystals form branches and combs.

Figure 9. A small portion from a children's pseudoephedrine chewable tablet (15 mg pseudoephedrine) after a chloroform extraction and 5 µL of $HAuCl_4$ reagent. Crystals form branches and combs.

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Pseudoephedrine: Gold Chloride (continued)

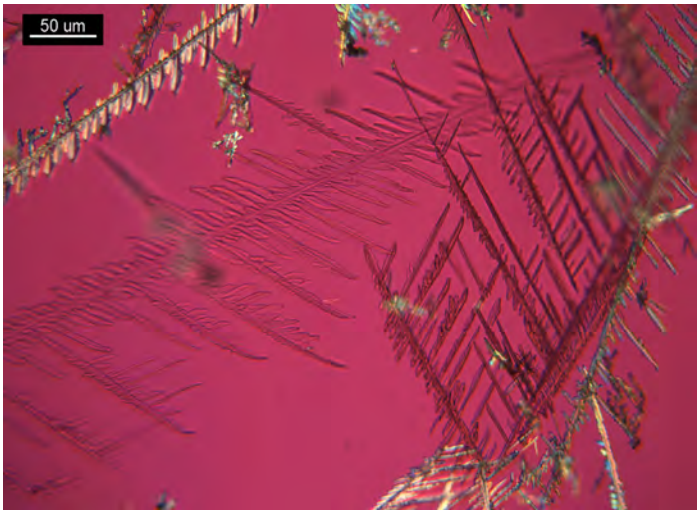

Figure 10. 1 PPP from a Wal-Phed® pharmaceutical tablet (60 mg pseudoephedrine HCl and 4 mg chlorpheniramine maleate) and 5 µL $HAuCl_4$ reagent. Crystals form branches and combs. Note symmetrical extinction: Vibration directions bisect the prominent crystal angle between crystal branches; crossed polars and Red I compensator.

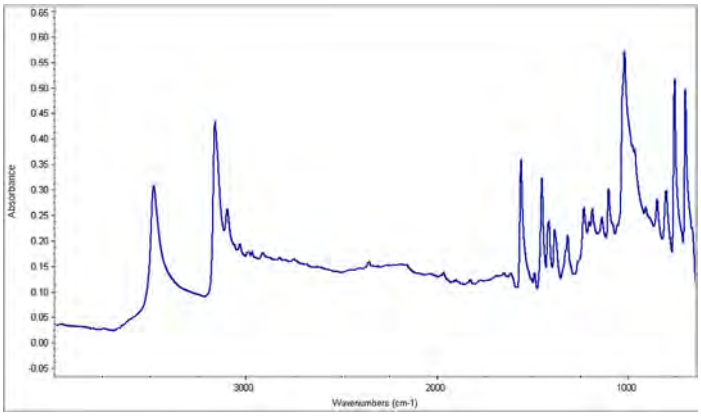

Figure 11. Infrared spectrum of pseudoephedrine gold chloride precipitate. Download SPC file.

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Psilocin: Trinitrobenzoic Acid

REAGENT 1: Trinitrobenzoic Acid

Trinitrobenzoic acid, saturated aqueous solution.

Test Method

Direct test: After extraction procedure, add 2 µL of reagent directly to sample on a glass side. Alternatively, dissolve sample in 2 µL of 1% HCl, then add 2 µL of reagent directly to the test drop. Note: Microcrystal tests for psilocin cannot be performed directly on mushrooms, therefore, a 2–3 hour extraction procedure must be performed to separate and isolate the psilocin.
See extraction procedure for separating and isolating psilocin on the following page.

References

1. Clarke, E.G.C. *Isolation and Identification of Drugs, Vol. 1*, The Pharmaceutical Press: London, 1969.
2. Casale, J.F. "An Aqueous-Organic Extraction Method for the Isolation and Identification of Psilocin from Hallucinogenic Mushrooms," *Journal of Forensic Sciences*, 30:1, pp 247–250, January 1985.
3. Beug, M.W. and Bigwood, J. "Quantitative Analysis of Psilocybin and Psilocin in *Psilocybe Baeocystis* (Singer and Smith) by High Performance Liquid Chromatography and by Thin Layer Chromatography," *Journal of Chromatography A*, 207:3, pp 379–385, 1981.

Limit of Detection

2 PPP

Time Required for Crystal Formation

≈ 20 minutes

Crystal Morphology and Test Notes

Red/brown drops form immediately, followed by rosettes of needles and blades, which form after ≈ 20 minutes.

Photomicrograph of Typical Crystals

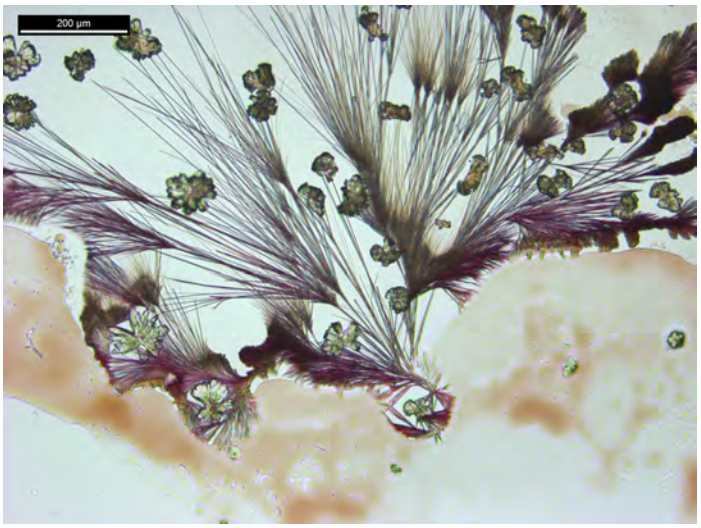


Figure 1. 2 PPP of psilocin after extraction and 2 µL of trinitrobenzoic acid reagent. Crystals form sheaves and fans of needles.

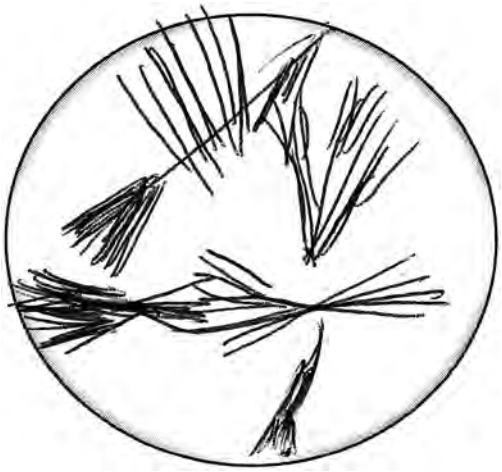
Pharmaceuticals, Adulterants or Other Drug Interactions

Psilocin and bufotenine can be difficult to distinguish using gas chromatography-mass spectroscopy (GC-MS), and they both form crystals with trinitrobenzoic acid reagent. However, bufotenine with trinitrobenzoic acid is orange and forms needles and blades (Figures 5–7). Psilocin with trinitrobenzoic acid is red and forms rosettes of needles and blades (Figures 1–4).

IR Spectrum

See Figure 8. Download SPC file.

PLM Optical Properties

Approximate Size Range	2–50 µm width; 10 to > 100 µm length
Color/Pleochroism	Red. Pleochroic: red (parallel) to orange-pink (perpendicular)
Refractive Indices (RI)	n-parallel ≈ 1.600 n- perpendicular > 1.700
Morphology Illustration	 *not to scale*
How Crystals Were Dried for RI Measurement	Crystals were dried at room temperature then washed with amyl acetate.
Estimated Birefringence	High
Extinction	Parallel
Sign of Elongation	Negative (–)
Crystal Optics and Optic Sign (Interference Figure)	Indeterminable

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Psilocin: Trinitrobenzoic Acid (continued)

Test Method

Continued from preceding page

Extraction procedure for separating and isolating psilocin (Casale, 1985):

1. Grind 2–10 g of dried mushrooms to a fine powder with a mortar and pestle.
2. Put mushroom powder into a 250 mL beaker and add 100 mL dilute acetic acid.
3. Adjust to pH 4 with glacial acetic acid and allow to stand for 1 hour.
4. Place beaker in boiling water bath for 8–10 minutes or until temp of mixture reaches 70° C.
5. Remove beaker and cool to room temp under running water.
6. Set up for vacuum filtration — plug funnel with glass wool (or use very coarse filter paper) and filter mixture.
7. To the filtrate add concentrated ammonium hydroxide, dropwise, to adjust to pH 8.
8. Transfer to separatory funnel (or use a stir bar, then transfer to separatory funnel), add 50 mL of diethyl ether, roll gently (do not shake) and decant off ether portion into 250 mL flask.
9. Repeat Step 8 with another 50 mL of diethyl ether.
10. Add anhydrous sodium sulfate directly into flask of ether extract and swirl. When the sodium sulfate has extracted all of the water, there will be some free crystals (not all clumpy).
11. Filter through filter paper into a beaker.
12. Place beaker into fume hood and allow to evaporate. Alternatively, pour the filtered extract into an evaporating dish, place evaporating dish into the fume hood and allow to evaporate.
13. After evaporation, there should be a greenish residue, it may be possible to perform microcrystal tests on this, or it can be re-crystallized by the following procedure: Add a small amount of a (1:3) chloroform:heptane (e.g. 0.5 mL and 1.5 mL heptane).

There are some important considerations when testing for psilocin: The quantity of psilocin in the mushroom, and the ability to identify it with microcrystal tests, is dependent on several variables. These variables include the mushroom growing conditions, sample age and storage conditions. It has been noted (Beug and Bigwood, 1981) that some dried mushroom herbarium samples lost all detectable psilocin after 1 year.

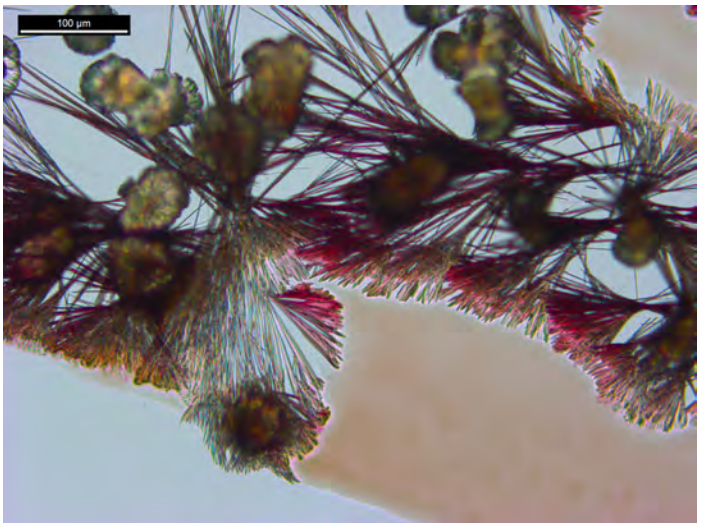

Figure 2. 2 PPP of psilocin after extraction and 2 µL of trinitrobenzoic acid reagent. Crystals form sheaves and fans of needles.

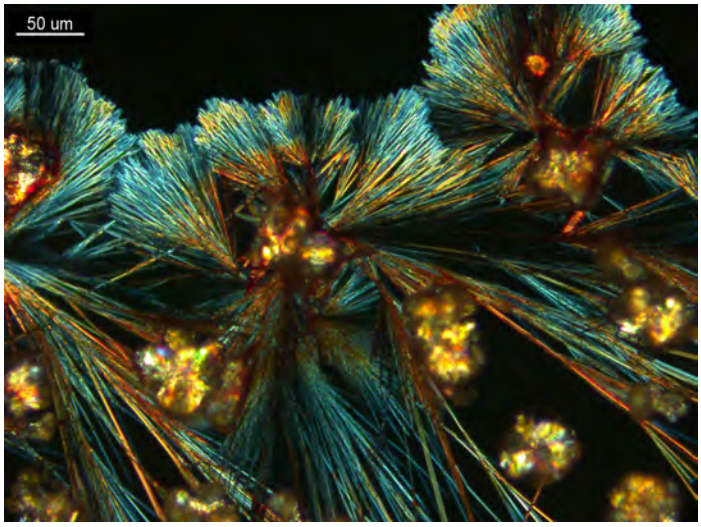

Figure 3. 2 PPP of psilocin after extraction and 2 µL of trinitrobenzoic acid reagent; crossed polars. Crystals form sheaves and fans of needles.

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Psilocin: Trinitrobenzoic Acid (continued)

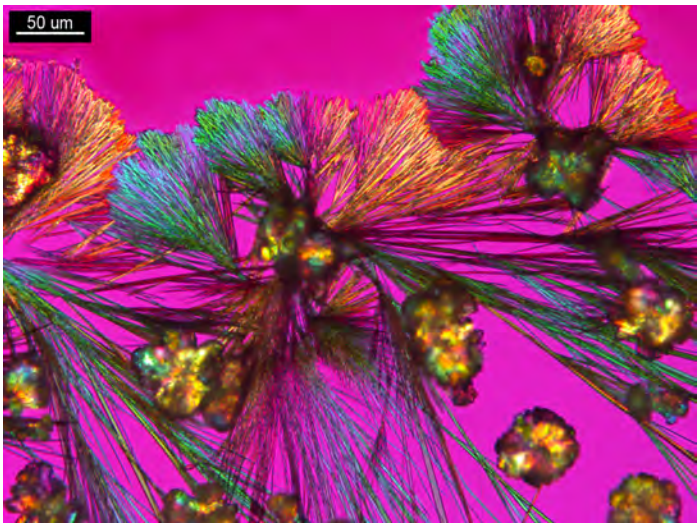

Figure 4. Same as Figure 3; crossed polars and Red I compensator.

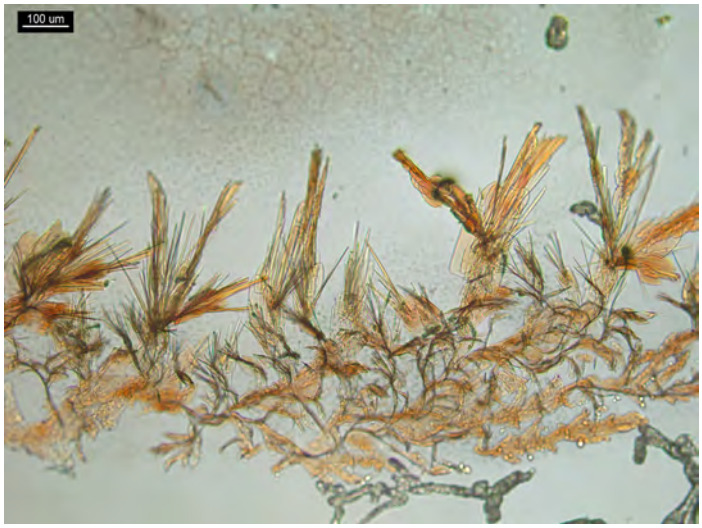

Figure 5. 2 PPP of bufotenine and 2 µL of trinitrobenzoic acid reagent. Crystals are orange needles and blades.

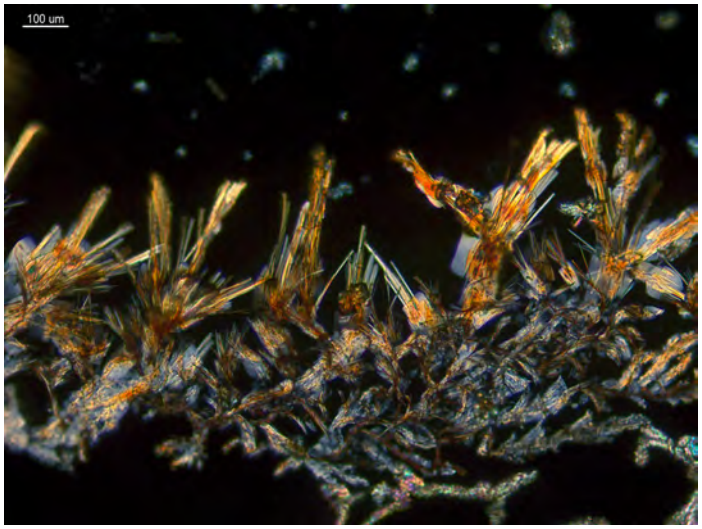

Figure 6. Same as Figure 5; crossed polars.

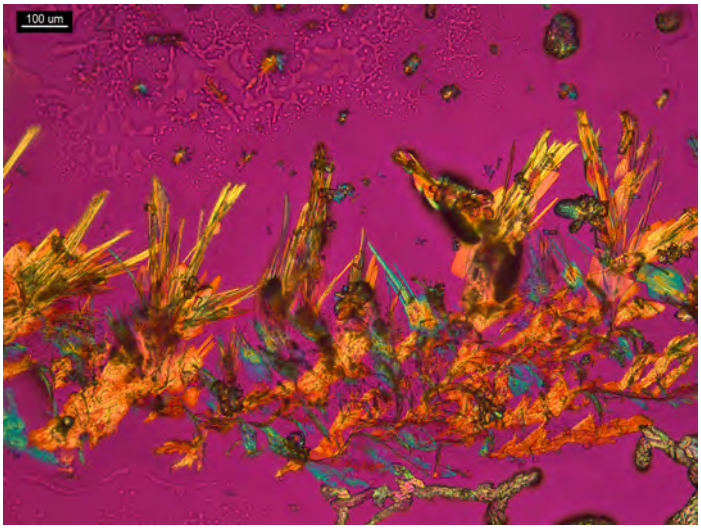

Figure 7. Same as Figure 5; crossed polars and Red I compensator.

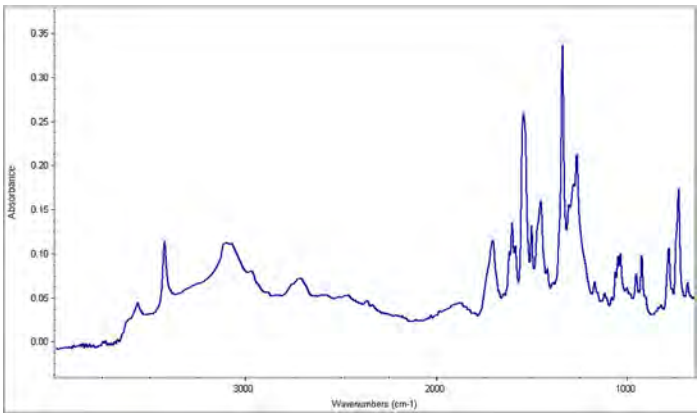

Figure 8. Infrared spectrum of psilocin trinitrobenzoic acid precipitate; sheaves of needles. Download SPC file.

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