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Purity Profiles for Heroin, Morphine, and Morphine Hydrochloride

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Abstract ☐ Purity profiles were established for samples of heroin (diacetylmorphine), morphine, and morphine hydrochloride in order to define the scope of utility of each as qualitative and/or quantitative analytical standards. Systems for solubility analysis and high-pressure liquid chromatography were investigated. A heroin synthesis affording a product of high purity is described.

Keyphrases ☐ Purity profiles—heroin, morphine, and morphine hydrochloride, phase solubility analysis, high-pressure liquid chromatography ☐ Heroin—synthesis, purity profile, phase solubility analysis, high-pressure liquid chromatography ☐ Morphine and hydrochloride salt—purity profiles, phase solubility analysis, high-pressure liquid chromatography ☐ Phase solubility analysis—purity profiles for heroin, morphine, and morphine hydrochloride ☐ High-pressure liquid chromatography—analysis, purity profiles, heroin, morphine, and morphine hydrochloride

Increased concern in recent years has given rise to demands for greater specificity and accuracy of analytical procedures for various abuse drugs, notably morphine and heroin. Along with this arises a need for standards for these drugs, having known scopes of utility for known qualitative and quantitative applications. The purposes of this report are to identify analytical procedures of value in determining the purity profiles (1) of these drugs and to define the analytical utility of given samples of the drugs. A synthesis of heroin is described which has yielded material suitable for use as an analytical standard.

METHODS AND MATERIALS

Morphine and its hydrochloride salt were obtained commercially. All reagents used were USP, NF, or ACS grade, except as noted.

Phase Solubility Analysis (2)—The method described in NF XIII (3) was followed. Nine 10-ml. tared glass ampuls were flushed with nitrogen, charged with an appropriate progression of sample weights and a fixed volume (3 ml. by pipet) of solvent, and flame sealed. All solvents were freshly distilled and degassed, starting with spectroquality or commercial distilled-in-glass grades. The bath temperature was 25°, the time allowed for equilibration varied with the drug, and rotation was 28 r.p.m. The residues obtained were dried to constant weight at 130°, except for heroin which was dried at 105°. All samples were kept in the dark when possible or in subdued light. The appropriate Student's *t* value, two-tailed, was used in calculating (2) the 95% confidence limits. In computing and

graphing the system composition, the sample weights used were converted to the anhydrous basis.

Titrations—Commercial equipment[1] was used for all potentiometric titrations (*n* = 3, averages given in Table 1) and the dead-stop end-point titration (duplicates).

Nonaqueous Titration (4a, 5)—The sample was dissolved in 5 ml. of glacial acetic acid and titrated to the potentiometric end-point with 0.1 *N* acetous perchloric acid, using a glass indicating electrode and a calomel reference electrode filled with 0.02 *N* lithium chloride in glacial acetic acid. The titrant was standardized against dried potassium biphthalate. Five milliliters of glacial acetic acid served as a blank.

Chloride—The sample was dissolved in 5 ml. of 1.5 *N* sulfuric acid and was titrated to the potentiometric end-point with 0.1 *N* silver nitrate, using a silver indicating electrode and a mercurous sulfate reference electrode. The titrant was standardized with dried sodium chloride, and 5 ml. of 1.5 *N* sulfuric acid served as a blank.

Moisture (4b, 6, 7)—An aliquot of sample was dissolved in anhydrous methanol, injected into a vessel containing methanol titrated to the end-point, and titrated with Karl Fischer reagent[2], using the dead-stop end-point technique and a 20-sec. delay. An aliquot of methanol was titrated as a blank. The titrant was standardized by titrating known volumes of water, delivered by gravimetrically calibrated microsyringe. Loss on drying to constant weight was determined on 300-mg. samples at 130°, except for heroin which was dried at 105°.

Spectroscopy—Recording UV[3] and IR[4] spectrophotometers were used to obtain spectra of the samples, and rotation data were obtained using an automatic polarimeter[5]. Absorptivity data in Table I are the averages of triplicates and rotational data are the averages of duplicates.

GLC—The GLC system[6] was as follows: on-column injection; 1.2-m. × 4-mm. i.d. glass columns; methylsilicone gum on silanized, acid-washed, flux-calcined diatomite; cured, conditioned, and tested as described previously (8); helium carrier gas at 50 ml./min.; flame-ionization detector; and automatic digital integrator[7] for area normalization. Temperature programs were 150–250°, and isothermal purity determinations were at 210°. A nonlinear adsorption graph was prepared for 0.5–100-mcg. sample injections of morphine, codeine, heroin, acetylcodeine, and both acetylmor-

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Table I—Purity Profile Data[a]

Test	Heroin	Morphine	Morphine Hydrochloride
Phase solubility analysis	99.9 ± 0.7%	99.6 ± 0.4%	See *Discussion*
Titrations			
Acetous perchloric acid	100.5%	100.2%	103.1%
Chloride	—	—	102.9%
Moisture (Karl Fischer)	0.03%	(6.1%)[b]	(14.4%)[b]
Loss on drying	0.03%	(6.1%)[b]	(14.3%)[b]
Chromatography			
GLC	99.8% a/a (two minor peaks)	99.9% a/a (two minor peaks)	99.9% a/a (one minor peak)
HPLC	≥99.8% a/a	≥99.5% a/a	≥99.8% a/a
TLC	One spot	One trace impurity	One trace impurity
Differential scanning calorimetry	<0.01 mole % eutectic impurity; ΔH = 7430 cal./mole; C.F. = 0.4%; T_0 = 446.9 °K.	Decomposes	Decomposes
IR	0.5% in KBr	0.5% in KBr	0.5% in KBr
UV absorption			
$A_{1\,cm}^{1\%}$ (max.)	47.8 at 278 nm.	52.7 at 285 nm.	46.5 at 285 nm.
Ratio (max./min.)	5.22 (in 0.1 N HCl)	3.38 (in 0.1 N HCl)	3.33 (in 0.1 N HCl)
Specific rotation			
$[\alpha]^{25}$, 589 nm.	−147.2°	−140.0°	—
578 nm.	−154.0°	−146.9°	—
546 nm.	−175.3°	−167.6°	...
436 nm.	−303° (0.5% in 0.015 N HCl-methanol)	−292° (1% in methanol)	—

[a] Values reported on anhydrous basis. [b] Morphine was the monohydrate (theoretical − 5.9%) and the hydrochloride was the trihydrate (theoretical = 14.4%), with moisture values on the as is basis.

phines. Morphine exhibited a trailing factor of 1.5 at 5% of peak height and efficiency, n = 1500; greater efficiency, n = 2600, was observed for heroin which, in contrast, did not trail. At the 100-mcg. injection level, heroin showed overload effects.

High-Pressure Liquid Chromatography (HPLC)—The HPLC system[8] was as follows: low-pressure mercury, 254-nm., UV detector; electronic integrator[7] for area normalization; and 1.0-m. × 2.2-mm. i.d., prepacked, stainless steel columns. The conditions tried were: (a) 40% methanol in water–chemically bonded ether on porous silica, 45°, 600 p.s.i.; and (b) pH 8.6 phosphate buffer–octadecylsilane on porous silica, 50°, 850 p.s.i. Strong cation-exchange experiments used a chemically bonded sulfonated fluorocarbon polymer. All solvents were filtered through suitable membrane filters and degassed prior to use.

TLC—Each undried sample was dissolved in methanol and 200, 100, and 20 mcg. were applied with micropipets (Drummond) to glass plates precoated commercially[9] with: (a) a 0.25-mm. layer of silica gel containing a fluorescent indicator, or (b) a 0.10-mm. layer of microcrystalline cellulose containing a fluorescent indicator. Sample application was made in subdued light, and the spots were dried in a stream of nitrogen and developed to a height of 10 cm. in the dark in glass chromatographic tanks containing one of the seven mobile phases listed. Spots were visualized by one or more of the five agents. Due to the low abundances of organic impurities in these samples and the lack of a common visualization agent, high-low TLC as described elsewhere (1) was not applicable. Some systems (II, III, V, VIII, and IX) were obtained from general references (9, 10). Relative mobility, R_f, of the main spots only are given here.

Systems for Morphine and Its Salt—The systems used were:

I. Glacial acetic acid–ethanol–water (3:6:1), R_f 0.52
II. Methanol–25% ammonium hydroxide (200:3), R_f 0.32
III. Ethanol–pyridine–dioxane–water (10:4:5:1), R_f 0.22
IV. Methanol, R_f 0.30 (cellulose)
V. Benzene–dioxane–ethanol–25% ammonium hydroxide (10:8:1:1), R_f 0.10
VI. Dimethylformamide–ethyl acetate (1:3), R_f 0.25

Systems for Heroin—The systems used were:

VII. Glacial acetic acid–ethanol–water (3:6:1), R_f 0.44

VIII. Methanol–25% ammonium hydroxide (200:3), R_f 0.38
IX. Benzene–dioxane–ethanol–25% ammonium hydroxide (10:8:1:1), R_f 0.46
X. Methanol, R_f 0.38
XI. 2-Propanol–water–glacial acetic acid (8:1:1), R_f 0.72 (cellulose)

Visualization (All Samples)—The following were used: long wavelength UV light (366 nm.), short wavelength UV light (254 nm.), iodine in chloroform spray (0.5%), acidified iodoplatinate spray (0.25 g. of platinic chloride and 5 g. of potassium iodide dissolved in sufficient water to make 100 ml. with 2 ml. of hydrochloric acid added), and acidified iodoplatinate spray followed by exposure to ammonia vapor.

Differential Scanning Calorimetry—Thermograms were recorded[10] from 80° to beyond the melting or decomposition points using microsamples in nitrogen-flushed, open pans.

Heroin Synthesis—Morphine monohydrate (the lot analyzed herein, 350 g., 1.154 moles) and acetic anhydride (99+%; 1095 ml., 1185 g., 11.6 moles) were placed in a 2-l. conical flask, and the resulting suspension was placed on a steam bath and kept at a temperature of 90° for 3 hr. The dark red-brown solution obtained was allowed to stand at room temperature for 3 days. All liquid (acetic acid and acetic anhydride) was removed with a rotary evaporator over a boiling water bath. Sufficient water was added to the solid residue to give an aqueous suspension with a volume of about 2.4 l. The aqueous suspension was cooled in an ice bath and made basic by slow addition, with stirring, of 5% aqueous sodium carbonate.

The pinkish-tan solid which precipitated was collected by filtration, washed twice with water, air dried, and powdered to give 419.4 g. of crude heroin base. Two recrystallizations from acetone afforded 117.9 g. of heroin base as a white crystalline powder, m.p.[11] 173.8–174.7°; molecular ion[12] m/e 369.

Second and third crops of heroin base were isolated from the combined recrystallization filtrates. The second crop consisted of 197.8 g. of a cream-colored crystalline powder, m.p. 172.5–174.1°, and the third crop consisted of 35 g. of a pale-tan crystalline powder,

[8] DuPont model 820 fitted with gradient elution accessory. Column packings were of the same manufacture; an ethereal polymer (ETH), octadecylsilane (ODS), and SCX Permaphase on Zipax support.
[9] E. Merck adsorbents from Brinkmann.

[10] DuPont model 990 thermal analysis unit fitted with the DSC head.
[11] Mettler FP2 apparatus with an FP21 microfurnace.
[12] Hitachi Perkin-Elmer RMU-6L mass spectrometer, 70 ev. ionizing potential.
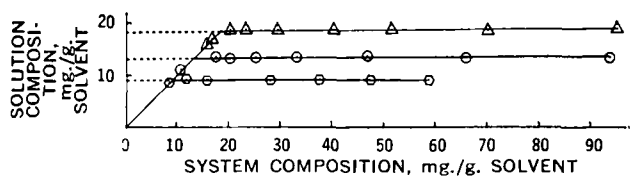
Figure 1—*Phase solubility diagrams of:* △, *morphine monohydrate in 2:1 methanol-ethanol, solubility (intercept)* = *18.4 mg./g., slope (soluble impurity)* = *0.38* ± *0.37%, undissolved phase was the monohydrate;* ○, *heroin in 3:1 hexane-dioxane, solubility* = *13.3 mg./g., slope* = *0.07* ± *0.71%; and* ⊙, *morphine hydrochloride (anhydrous) in ethanol, solubility* = *9.2 mg./g., slope* = *−0.07* ± *0.85%, undissolved phase was the anhydrous.*

m.p. 171.6–173.5°. A total of 350.7 g. (82.3%) of heroin base was obtained.

RESULTS AND DISCUSSION

Heroin (Diacetylmorphine)—Heroin was prepared by acetylation of morphine with acetic anhydride in a manner similar to reported syntheses (11–16). Morphine and acetic anhydride were reacted in direct mixture to form the acetate salt of heroin. The heroin base was then isolated from aqueous sodium carbonate and purified by two recrystallizations from acetone. Product identification was verified by reference to published IR, UV, and rotation data (9, 17–19), in addition to the molecular ion and melting point. Literature melting points vary over a range of 169–173° (12–16).

Solubility analysis was achieved, after several attempts, with 3-day equilibration in a dry hexane-dioxane mixture (Fig. 1). GLC analysis of the undissolved crystals and the residue from the supernate showed that hydrolytic decomposition had not occurred. It is important that the dioxane used be freshly treated with iron dust (20) followed by activated charcoal to remove any peroxides and then distilled to give a dry, residue- and peroxide-free fraction. Solubility analysis in diluted ethanol, 55% in degassed water, failed due to hydrolytic decomposition: 8% after 1 day as determined by GLC. Insoluble impurities were not present in either solubility system. Analyses by GLC of the two phases of the latter system showed that the hydrolysis products did not form solid solutions.

Titrimetric and calorimetric purity data were consistent with the assay by solubility analysis. TLC did not reveal any impurities. Calculation of apparent eutectic impurities was done by the usual Van't Hoff relationship discussed elsewhere (1). Remelt of a sample showed, by the appearance of a probable eutectic endotherm at 4° less than the melting point, that some thermal decomposition had occurred on melting the sample, even under nitrogen.

UV-absorbing impurities were not detected (Fig. 2) by HPLC, using gradient elution in the adsorption-cation-exchange mode. Morphine, codeine, and both acetylmorphines are eluted more rapidly than heroin in this system, the most desirable situation for purity evaluations. These impurities (≤ 0.2%) were ruled out for this sample. The order of elution is that of decreasing polarity of substituents and, presumably, decreasing solubility in the aqueous salt solution. Heroin, 200 mcg., gave 0.065 absorbance unit peak height, with overload effects apparent. Calibration mixtures of O^6-acetylmorphine in heroin exhibited a rectilinear relationship in the peak height ratio (0.05 height ratio unit per 1% impurity). Because HPLC is in an early stage, it was deemed prudent to test the reliability of this system. Three other packed columns, from other laboratories, were tested in this laboratory with similar results. Figure 2 represents intermediate performance.

Acetylcodeine, an important heroin impurity, eluted just prior to heroin and can be estimated only when present in abundance, as is the case for the mixture of authentic drug substances in Fig. 2. Acetylcodeine was completely overlapped by the heroin peak when present to the extent of a few percent, so that GLC would be preferred for the measurement of this impurity in the usual illicit samples of heroin.

Cashman and Thornton (21) reported an adsorption–liquid chromatographic separation of heroin, O^6-acetylmorphine, and morphine, in that order of elution. Unfortunately, heroin eluted first and was poorly separated from acetylmorphine, rendering the system less useful for purity or stability work.

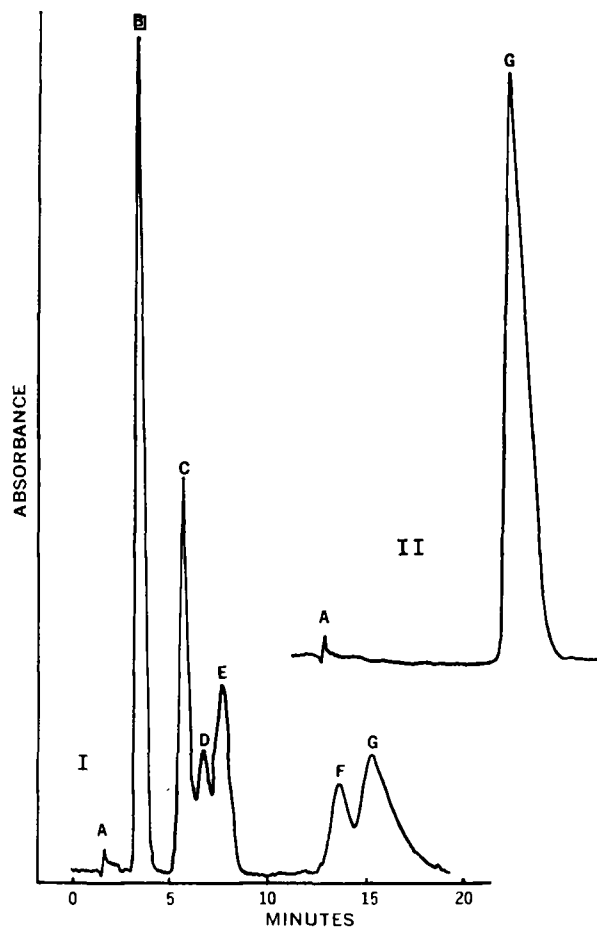GLC revealed two unresolved peaks (total area 0.15%) at 0.65–

Figure 2—*High-pressure liquid chromatograms of: I, authentic mixture; and II, analytical sample. Key: A, solvent; B, morphine; C, O^6-acetylmorphine; D, O^3-acetylmorphine; E, codeine; F, acetylcodeine; and G, heroin. Gradient elution 0.4–1.4 M sodium perchlorate in 0.01 M pH 6.8 aqueous phosphate buffer containing 10% ethanol; 35°; SCX, 1000 p.s.i.*

0.70 relative retention, which were the two acetylmorphines. This system almost separated them[13] [resolution factor (8) ~0.7]. This level is too low for reasonable correction for nonlinear adsorptive losses. No acetylcodeine was evident in the sample, as would be expected for a sample prepared from morphine of defined purity.

The HPLC system is to be preferred over GLC for determining the morphine and acetylmorphine contents of heroin unless several percent of impurities is present so that reasonable correction for nonlinear adsorptive losses can be made. Such losses are characteristic of phenols and commonplace for compounds with several polar functional groups, i.e., morphine and its polar derivatives. It is also characteristic that individual chromatographic systems vary widely in this regard. Because any derivatization step can be the occasion either of purification or decomposition, purity values by such methods (except where a separately defined standard is examined concomitantly) are not considered reliable, even though they may be the basis of entirely satisfactory assay procedures once a standard is otherwise established.

All these purity profile data showed this sample of heroin to be satisfactory for use as an analytical standard in qualitative and quantitative applications.

Morphine Monohydrate—Phase solubility analysis (Fig. 1), using 6-day equilibration, indicated that this sample of morphine was essentially single-component material. Nonaqueous titration results (Table I) were consistent with this indication. The base and hydrochloride were characterized by UV (17) and IR spectropho-

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[13] O^3-Acetylmorphine at 0.66, acetylcodeine at 0.68, and O^6-acetylmorphine at 0.71. For comparison, on OV-17/Q these relative retentions (heroin = 1.0) are 0.58, 0.56, and 0.59, respectively, but higher temperatures make this even less desirable as a phase. Silylation (bistrimethylsilylacetamide) does not improve this situation.

tometry (9, 18) and optical rotation (19). The spectra were found to be similar to published spectra and identical to those of another dried sample of morphine.

TLC showed the material to be nearly homogeneous using six systems. One small but distinct impurity was detected which appeared as a yellow fluorescent spot having the approximate mobility of papaverine (orange fluorescence), indicating the possible presence of such a benzylisoquinoline. Semiquantitation (1) was not feasible due to the lack of a common visualization agent. Within the morphine spot was an area of blue fluorescence not separable from the main spot by any solvent system tried; this was interpreted to be pseudomorphine, an artifact (22) of on-plate oxidation, particularly in the presence of ammonia. Two-dimensional TLC did not reveal any additional artifacts.

Temperature-programmed GLC revealed no impurities of greatly different vapor pressures in the morphine sample. Isothermal purity determination showed the two impurities (Table 1) at relative retentions of 0.94 and 4.2, respectively. The retentions of the two impurities resembled those of papaverine and codeine. Spiked samples indicate that the larger impurity may be codeine and the same experiment tends to exclude papaverine. It is not possible at such low levels of impurities to exclude firmly or identify likely impurities without mass spectrograms of the eluted peaks; for example, reagent rather than spectroquality chloroform gives a peak at the same locus as codeine.

In the HPLC of morphine, three packings[14] were tried in both normal and reverse phase modes. Although these packings are among the most reliable available, none yields ideal peak shapes, and substantial adsorptive trailing precluded exact quantitation. Exchange resins also were investigated. Only the reverse phase systems yielded interpretable chromatographic purity data. Electronic area integration did not give useful data because of the contribution of trailing-in from earlier peaks. The single impurity peak had the same mobility as codeine and it is estimated that this is less than 0.5%.

Samples of both dried and undried material were examined by differential scanning calorimetry. Due to decomposition, however, no purity estimate can be made. The undried sample showed a substantial endotherm in the 110–140° region, which represents the removal of water, and a sharp endotherm at about 260° with severe decomposition. A sample dried at 50° *in vacuo* showed only traces of the lower endotherm, and a sample dried at 130° lacked this endotherm completely. No attempt was made to prepare or identify different polymorphs, although polymorphism has been observed for this drug[16].

Drying of morphine monohydrate at 130° was shown by differential scanning calorimetry and Karl Fischer titrimetry to remove all moisture from the sample, and TLC of the dried material indicated no decomposition. Drying of this material, in small amounts for quantitative use, at 130° for 2 hr. in static air is, therefore, recommended.

The purity profile afforded by these data allowed the recommendation of this sample of morphine monohydrate as an analytical standard for both qualitative and quantitative applications.

Morphine Hydrochloride Trihydrate—This sample was found to be nearly homogeneous by TLC with six solvent systems, and these results were essentially the same as those reported for morphine.

Prior to GLC, the hydrochloride salt was converted to the free base by extraction from pH 9.5 buffer into a 10% solution of 2-propanol in chloroform. This same solvent mixture also was used for morphine. Isothermal operation revealed one impurity with a relative retention of 0.94, and temperature programming revealed no additional impurities. Spiked samples suggested that this impurity was codeine, but at such low abundances that positive identification is difficult. HPLC located one minor impurity, similar to that in the morphine sample.

Nonaqueous titration (Table 1) of morphine hydrochloride required that mercuric acetate be added to the titration medium to convert all chloride salts to titratable bases; however, in this system any alkali metal or ammonium ions present also titrate as bases (5), contributing by a disproportionately large amount to the total titration value. Taken with the high chloride content, titrimetry

clearly indicates lower molecular weight impurities. The moderate pH value (4.7 using a 2% aqueous solution) excluded excess hydrochloric acid as a significant factor. Chromatographic analyses showed a lack of substantial organic impurity. Inorganic chlorides were indicated, and some sodium was shown to be present by a classic flame test.

Samples of both dried and undried material were examined by differential scanning calorimetry. Due to decomposition, however, no purity estimate was possible. In the 60–110° range, two endothermic peaks were found. No evidence was found of a main melt in the 50–260° range by this technique. A scan of material dried at 50° *in vacuo* showed a slight trace of the two endotherms, whereas material dried at 130° lacked these peaks completely. When taken together with the titrimetric moisture and comparative TLC results, these results substantiate the complete removal of moisture and lack of significant degradation at 130°. The moisture content was found to be consistent with the expected trihydrate form, but the material should be dried prior to use as a semiquantitative standard.

An initial solubility analysis in alcohol (10-day equilibration) gave 2.2 ± 0.4% slope; however, anhydrous drug was isolated as the undissolved phase whereas the trihydrate was used as the sample, indicating that solvent composition was not constant. Coupled with common-ion effects of the inorganic chlorides, this rendered the slope uninterpretable[16] (23), and this slope value was ignored in constructing the purity profile of the sample. An 8-day equilibration of previously dried sample gave a −0.1% slope. Because titrimetry revealed lower equivalent weight chloride salts in the sample, this slope also cannot directly reflect sample composition because the excess chloride equivalent can exert a common-ion effect on the slope that is opposite to the mass impurity effect. Titrimetric values and this latter slope are consistent with the equivalent of 0.5–0.6% sodium and ammonium chlorides.

These data are interpreted as representing an organically pure sample of morphine as the trihydrated hydrochloride salt which contains inorganic material. This would not impair the qualitative utility of this standard. The morphine monohydrate, because of its single-component composition, would be required for *quantitative* use.

SUMMARY

Samples of heroin, morphine, and morphine hydrochloride were evaluated by phase solubility analysis, titrimetric moisture, loss on drying, nonaqueous titration, chloride titration, UV and IR absorption, differential scanning calorimetry, optical rotation, GLC, TLC, and HPLC.

Systems for solubility analysis and HPLC were developed in support of this work. A synthetic method yielding heroin of a high degree of purity is reported.

The purity profiles established for each sample allowed definition of the scope of utility of each as an analytical standard in either qualitative or quantitative applications.

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PHARMACEUTICAL TECHNOLOGY

Shear Cell Measurements of Powders: Determination of Yield Loci

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Abstract ☐ The usefulness of the Jenike-type shear cell and associated procedure for the characterization of some powder bed properties has been established by others. An attempt to use a simpler procedure and a different shear cell and thereby to reduce the quantity of powder required is described. The yield loci obtained are very nearly linear. Multiple-regression analysis is used to obtain characteristic constants from the data for the family of yield loci. Examples of the data obtained for various pharmaceutical powders are presented.

Keyphrases ☐ Shear cell measurements—simplified determination of yield loci for powders ☐ Powder bed properties—simplified procedure and shear cell for determination of yield loci

It is postulated that the flow of powder occurs when the forces acting on a powder bed cause the resultant shear force just to exceed the powder bed's shear strength in any given direction. Therefore, the flow characteristics of the powder can be described in terms of an orthogonal set of principal forces. Only two, the major and minor forces, have a significant effect on the location of the shear plane. The magnitude of these forces depends upon the state of consolidation of the powder bed. For many applications, it is adequate to describe the changes of unconfined powder bed properties with the change in the state of consolidation. This description is in the form of a failure function, a plot of the major stress necessary to cause failure of an uncon-

fined bed *versus* the major stress that produced the given state of consolidation.

The failure function can be estimated from shear cell data (1) or a triaxial test method (2); both methods usually fail to provide completely accurate evaluations. The shear cell methods are the most popular. This article briefly discusses the theory relating to these concepts and reports results of studies with a simple shear cell. Also included is a limited comparison of the data obtained with one sample using two different shear cells.

CONCEPTS

Figure 1 shows the direction of forces acting in both the triaxial test and the shear cell. It also shows the Mohr semicircle used to describe the stress balance at failure. With the triaxial method, the major stress, σ_m, and the minor stress, σ_s, are the applied stresses and τ and σ_n are the resultant stresses. Moreover, the angle α is observed, so the corresponding Mohr semicircle can be constructed. With the shear cell, σ_m, σ_s, and α are not determined; only τ and σ_n are known. Therefore, a single measurement does not provide enough information to permit construction of the corresponding Mohr semicircle. When σ_m and σ_s are of the correct magnitude to produce failure, *i.e.*, shearing of the powder bed, then τ and σ_n appear on the circle. As can be seen from Fig. 2, the principal stress, σ_i, which is intermediate in magnitude, does not influence the failure. The resultant τ and σ_n values represented by the Mohr semicircles involving σ_i are always less than any τ, σ_n values on the semicircle between the major and minor principal stresses. There-