

The importance of recognizing an interaction between corticosteroids and salicylates is obvious. However, it is unclear from these data that the interaction exists, at least in the dog. Hansten (6) listed this interaction, citing the paper by Klinenberg and Miller (4). Their paper also was cited in a symposium on chronic salicylate therapy, but it was pointed out that their results were unconfirmed (7). Our results, showing that corticosteroids did not lower plasma salicylate concentrations in dogs, suggest the need to examine further the reported interaction between these drugs in humans.

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Spot Tests Used for Systematic Identification of Drugs of Abuse

Keyphrases □ Drugs of abuse—systematic identification using spot tests □ Abuse drugs—systematic identification using spot tests □ Spot tests—systematic identification of drugs of abuse

To the Editor:

A number of the observations reported by Masoud (1) are at variance with long accepted literature results (2-6) and our own observations. Our observations are based on tens of thousands of forensic samples which come into our laboratory each year and which are screened using the spot tests mentioned in Masoud's paper (1).

To ensure that these inconsistencies were not due to small differences in the composition of the spot test reagents commonly used in our laboratory and those of Masoud, we prepared reagents to the specifications of Masoud's paper. The observations reported here are based on these reagents. Samples in the range described by Masoud, i.e., 1-2 mg, were used, and all tests were run in porcelain spot plates. The following serious inconsistencies were encountered.

1. In Table II of Masoud's paper under the caption "Alkaloids that Give Negative Tests with One or More Reagents":

(a) The table indicates that heroin and morphine give a positive Mayer, a positive Dragendorff, and a negative Wagner test. It is our observation that both give strong positive reactions with all three of these reagents.

(b) The table indicates that lysergide (LSD) gives negative results for all three of the alkaloidal tests. It is our observation that pure lysergide gives strong positives with these reagents. Some illicit samples, where the lysergide concentration is quite low, still give a positive Wagner test. The concentrations encountered in many illicit samples will be below the sensitivity limits of these spot tests.

(c) The table indicates negative tests with all three reagents for psilocybin. Our observation is that psilocybin gives a positive Wagner and a negative Mayer test.

2. In Table III, under the caption "Nonalkaloids that Give Positive Alkaloidal Tests with One or More Reagents": The table indicates that procaine and methylphenidate give a negative Mayer and a negative Wagner test. Our observation is that both these compounds give positive tests with both reagents.

3. In the discussion of the Marquis reagent on page 843:

(a) The discussion indicates that some nonopiates produce color reactions with the Marquis reagent very similar to those shown by the opiates. Ephedrine sulfate, amphetamine sulfate, methamphetamine hydrochloride, and meperidine are listed as examples. Our observation is that the colors produced by these compounds are not similar to the colors produced by the opiates. In fact, the orange to brown color reaction produced by ephedrine, amphetamine, and methamphetamine with the Marquis reagent is used in our laboratory and in most other crime laboratories as a screening test for these compounds (2-6).

(b) The discussion continues that these "false positives" are not documented in "other references known to the author." An extensive compilation of the colors produced with the Marquis reagent, which includes these compounds, is found in "Isolation and Identification of Drugs" (2), cited by Masoud as his Ref. 6. Furthermore, this information is in all modern references on forensic drug analysis (2-6).

4. In the discussion of cobalt thiocyanate on page 843: The author comments on the lack of specificity of this test in the identification of cocaine, due to other compounds giving the characteristic flaky pre-

cipitate. It is our observation that many other compounds do, in fact, produce this color reaction. However, a modification to the test, using stannous chloride solution (7), enhances the specificity.

For example, procaine, benzocaine, diphenhydramine, and cocaine do give a blue precipitate with cobalt thiocyanate reagent; but upon addition of stannous chloride solution, the blue precipitate disappears in the case of procaine, benzocaine, and diphenhydramine but remains unchanged with cocaine.

5. In the discussion of the Zwikker test on page 843: The discussion indicates that glutethimide gives a gray color with the Zwikker reagent, which is inconsistent with the blue-violet color reported by Clarke (2) for glutethimide and barbiturates. Our observations are in agreement with those of Clarke (2).

The reported results using reagents prepared according to the formulations in Masoud's paper (1) are in accord with our previous experience and the literature. Therefore, the inconsistencies between our experience and the results reported by Masoud cannot be due to small differences in the reagents used. We feel it is important that these observations be brought to the attention of the scientific community, since our chemists and those working in hundreds of other crime laboratories across the nation must defend their results in court under intense cross-examination. Frequently, under cross-examination, articles in the scientific literature at variance with the chemist's results are quoted to cast doubt on his or her credibility and to confuse the lay people of the jury.

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Spot Tests Used for Systematic Identification of Drugs of Abuse: A Response

Keyphrases □ Spot tests—systematic identification of drugs of abuse
□ Drugs of abuse—systematic identification by spot tests □ Abuse
drugs—systematic identification by spot tests

To the Editor:

The communication by Rorke *et al.* (1) in reference to an earlier paper (2) discussed a number of discrepancies between our results. We would like to deal with each point in the following discussion.

Wagner's Reaction with Heroin, Morphine, Psilocybin, Procaine, and Methylphenidate—The spot tests performed by Rorke *et al.* (1) were run in porcelain spot plates. This procedure is not in agreement with the use of small glass test tubes described in our work. This difference was found to be crucial since, in our laboratory, we shake the test tube upon the addition of the reagent as a general practice; this is not done when porcelain spot plates are used.

With the drugs of controversy, namely, heroin, morphine, psilocybin, procaine, and methylphenidate, when one or two drops of Wagner's reagent in the concentration used (1–2 mg) are added and the test tube is shaken, the initial precipitate disappears, which has caused the interpretation as a negative. However, we do agree with Rorke *et al.* that when spot plates are used and when three or more drops of Wagner's reagent are added, a positive reaction is observed.

Lysergide Detection and Reaction with Alkaloidal Spot Tests—In the original paper (2), under *Preparation of Samples*, it was mentioned that lysergide was detected in quantities as low as 5 µg. This concentration was used for the detection of lysergide by alkaloidal spot tests and the Ehrlich reagent. At these concentrations, lysergide is not detectable with all three alkaloidal reagents but is detectable with Ehrlich's reagent. Since many street samples contain concentrations below the sensitivity of the alkaloidal spot tests which are detectable by Ehrlich's reagent and for the sake of not missing such low concentrations, the worker should test the drug with Ehrlich's reagent even if it is negative to the alkaloidal spot tests. Rorke *et al.* (1) are correct, however, in pointing out that high concentrations of pure lysergide do give positive alkaloidal spot tests.

Reaction of Procaine and Methylphenidate with Mayer's Reagent—Procaine and methylphenidate formed a very slight precipitate with Mayer's reagent a few minutes after the reagent was added. This delayed, weak reaction differs from the instantaneous strong precipitate formed with most alkaloids. This difference was responsible for the controversy.

Marquis Reagent—In the earlier paper (2), it was mentioned that some nonopiates produced similar colors to those produced by opiates, and a few examples were given. Many of these colors are indeed very similar to those produced by opiates. For example, methapyrilene produces a black-purple color, as documented by

Clarke (3). Indeed, some colors produced by other drugs (e.g., ephedrine, amphetamine, and methamphetamine) may be identified by trained eyes, but untrained personnel should be warned of the possibility of misidentification, particularly when other extraneous material and colors are added to the drug as is the case with street drugs. As Clarke stated:

"The color given in any test depends on the quantity of material used and on its purity, and may be described differently by different individuals. To allow for this, the following lists must be used in as wide a sense as possible."

Therefore, it is up to the worker to exercise his or her judgment in utilizing such color tests for the primary screening of these compounds.

Clarke's compilation of the colors produced with the Marquis reagent did not include ephedrine (3).

Cobalt Thiocyanate—Table IV in the earlier paper (2) included 14 compounds that gave a blue flaky precipitate with cobalt thiocyanate. Rorke *et al.* (1) suggested the use of stannous chloride to enhance the specificity of the test by differentiating between cocaine and procaine and between benzocaine and diphenhydramine; however, they did not mention the behavior of the other compounds listed in the table or of the many other compounds not included. They also failed to consider that many street samples contain mixtures of cocaine and procaine, which make this test worthless or, at best, very difficult to interpret.

The addition of stannous chloride to the blue flaky precipitate formed by such a mixture results in partial dissolution of the precipitate. This partial dissolution is very difficult to observe, and the mixture may be misidentified as cocaine. Rorke *et al.* (1) also failed to mention that the blue precipitate formed by methadone dissolves only partially in stannous chloride, which adds to the possibility of erroneous interpretation.

Therefore, it is our opinion that the use of stannous chloride does not add to the specificity of this test and may lead to erroneous results. For these reasons, it was not included in the scheme described in the original paper (1).

Zwicker's Test—The original paper (2) is in disagreement with Rorke *et al.* (1) and Clarke (3). We repeated the experiment using the reagents described and amobarbital, phenobarbital sodium, and secobarbital as reference standards. At the concentration of 2 mg of the barbiturates used, an instant blue-violet color developed, which was found to be very stable. At this concentration, no blue-violet color was developed with glutethimide. Instead, a yellow color developed, which changed upon standing to a gray color. However, very high concentrations of glutethimide, *i.e.*, more than 10 mg, produced a similar blue-violet color, which disappeared almost instantaneously and faded to a gray color within a few seconds. Therefore, we stand firmly by the results reported earlier (1).

In conclusion, we feel that this exchange with Rorke *et al.* (1) has clarified a number of points, which are examples of the many scientific variables between laboratories due to human differences and differences in methodology. This exchange has also demonstrated, as

was pointed out previously (2), that these tests only provide preliminary information to help in the selection of the necessary confirmatory tests such as TLC and GLC. They also aid in the selection of the compound or compounds that are to be used as reference standards for the final identification by TLC or GLC.

Rorke *et al.* (1) pointed out the importance of such tests for chemists defending their results in the courts. We disagree with them in this statement. Results of spot tests should never be used as evidence in the courts.

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Intramolecular and Intermolecular Transformations of Aspirin in Nonhydroxylic Solvents

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To the Editor:

Much evidence has been presented (1-3) to suggest that the hydrolysis of ionized acetylsalicylic acid (aspirin) involves intramolecular general-base catalysis by the carboxylate anion and not, as previously supposed (4-8), an intramolecular nucleophilic catalysis with a kinetically significant intermediary formation of the mixed anhydride of salicylic and acetic acids. There seems, however, to be an equilibrium between acetylsalicylate and the anion of the mixed salicylic acetic anhydride (3, 9). But since the anhydride reverts to the starting ester much faster than it is hydrolyzed, the nucleophilic pathway is not a feasible hydrolytic route.

The hydrolysis of the ester group in acetylsalicylic acid is also catalyzed by the unionized carboxyl group (2, 10). In this case, nucleophilic catalysis may be involved because of a more favorable equilibrium constant for the formation of the protonated form rather than the ionized one of the mixed anhydride intermediate (10).

We have observed, and now wish to report, novel and unusual reactions of acetylsalicylic acid occurring in solutions of the acid in nonhydroxylic solvents.