

## Letter to the Editor

### Radioimmunoassay for Phencyclidine

Sir:

Recently, we reported [1] the development of a radioimmunoassay (RIA) for phencyclidine (PCP) that uses an  $^{125}\text{I}$ -labeled PCP derivative as antigen and anti-PCP serum induced in rabbits. Cross-reactivity of the reagents to 20 commonly prescribed drugs and to three compounds chemically related to PCP, 1-(1-phenylcyclohexyl)-4-hydroxypiperidine, phenylcyclohexylamine, and ketamine, was described. Eighteen additional phencyclidine analogs have since been obtained and it is the purpose of this communication to present the results of testing the RIA reagents for cross-reactivity with these compounds.

Reagents used in this study were identical to those described previously [1] and are now available as Abuscreen® RIA for Phencyclidine (Hoffmann-La Roche Inc., Nutley, N.J.).

All analogs tested were obtained through the cooperation of Dr. Richard Hawks, National Institute on Drug Abuse, Rockville, Md.

Each compound was dissolved in absolute ethanol to a concentration of 10 mg/mL. Serial dilutions of this stock were then prepared in pooled human urine known by RIA testing to be free of PCP. Appropriate dilutions of each analog, assayed in duplicate, produced concentrations that could be interpreted from the usable (0–200 ng/mL) portion of the response curve. The nanogram PCP equivalents per millilitre thus obtained were averaged and the ratio of PCP equivalents to analog concentration, corrected for hydrochloride content where required, was determined.

The PCP analogs are listed in descending order of cross-reactivity in Table 1. The most cross-reactive compound tested was 1-(1-phenylcyclohexyl)hexamethyleimine, which differs from phencyclidine only by the addition of one carbon atom into the piperidine ring. This addition reduces by more than 50% the ability of the antibody to recognize

TABLE 1—Cross-reactivity of phencyclidine (PCP) analogs.

| Compound  | Relative Cross-Reactivity <sup>a, b</sup> |
|---|---|
| 1. 1-(1-Phenylcyclohexyl)hexamethyleimine hydrochloride                 | 48  |
| 2. 1-(1-Phenylcyclohexyl)-4 methylpiperidine hydrochloride              | 19  |
| 3. 1-(1-(2-Thienyl)cyclohexyl)pyrrolidine hydrochloride                 | 15  |
| 4. 1-(1-Phenylcyclohexyl)-3 methylpiperidine hydrochloride              | 15  |
| 5. 1-(1-Phenylcyclohexyl)morpholine hydrochloride                       | 12  |
| 6. 1-(1-(2-Thienyl)cyclohexyl)morpholine hydrochloride                  | 7.0                                       |
| 7. 4-Phenyl-4-piperidinocyclohexanol                                    | 3.6                                       |
| 8. <i>N,N</i> -Diethyl-1-phenylcyclohexylamine hydrochloride            | 3.5                                       |
| 9. 1-(1-Phenylcyclohexyl)-4 hydroxypiperidine                           | 1.7                                       |
| 10. <i>N</i> -( <i>n</i> -Propyl)-1-phenylcyclohexylamine hydrochloride | 0.7                                       |
| 11. <i>N</i> -( <i>n</i> -Butyl)-1-phenylcyclohexylamine hydrochloride  | 0.3                                       |
| 12. <i>N,N</i> -Dimethyl-1-phenylcyclohexylamine hydrochloride          | 0.2                                       |
| 13. <i>N</i> -( <i>s</i> -Butyl)-1-phenylcyclohexylamine hydrochloride  | 0.2                                       |
| 14. <i>N</i> -( <i>i</i> -Propyl)-1-phenylcyclohexylamine hydrochloride | 0.2                                       |
| 15. <i>N</i> -Methyl-1-phenylcyclohexylamine hydrochloride              | 0.1                                       |
| 16. 1-Phenylcyclopentylamine hydrochloride                              | 0.0                                       |
| 17. 1-Phenylcyclohexylamine   | 0.0                                       |
| 18. 1-Piperidinocyclohexanecarbonitrile                                 | 0.0                                       |

<sup>a</sup>Based upon the ng equivalents for PCP as 100.

<sup>b</sup>Correction for hydrochloride content applied where necessary.

this compound as antigen. Replacements of the piperidine ring with morpholine, pyrrolidine, or thienyl groups, or additions of hydroxyl or methyl groups to the piperidine or cyclohexyl rings, result in significant (>80%) reduction in cross-reactivity. Removal of the three-ring structure virtually eliminates cross-reactivity.

The results shown here are consistent with those published previously [1] indicating extremely low (<0.01%) levels of cross-reactivity with the urinary metabolite of phencyclidine, 1-phenylcyclohexylamine. Results obtained with another metabolite, 1-(1-phenylcyclohexyl)-4-hydroxypiperidine were somewhat lower in this analysis than those previously reported for the metabolite obtained from a commercial supplier. Reasons for the difference are unclear at this time.

The third known metabolite of phencyclidine, 1-(3-hydroxy-1-phenylcyclohexyl)piperidine, is presently still unavailable. However, since addition of a methyl group into the 3 position (No. 4 of Table 1) or of a hydroxyl group into the 4 position (No. 9) results in 2 to 15% cross-reactivity, a similar degree of interaction with this compound would be expected.

Metabolites of PCP have been identified in urine at very low concentrations relative to the parent drug [2,3]. Consequently, the level of cross-reactivity to metabolites seen here should not hinder detection of PCP-positive urines and might be advantageous in clinical situations requiring determination of unmetabolized drug.

Additionally, compounds related to PCP, including thienyl, pyrrolidine, and *N*-ethyl analogs, have appeared illicitly on the street [4]. These substances are listed as Schedule I by the Controlled Substances Act and, thus, were not obtained for testing. However, cross-reactivity to these structural components is such that thienyl and pyrrolidine analogs might be detected when present in high (>1000 ng/mL) concentrations.

The authors welcome any additional information or comments concerning the performance of the RIA reagents towards these Schedule I analogs or towards any other drugs.

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#### References

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