Rapid g.l.c. method for the separation of picogram quantities of morphine and codeine

M. J. KOGAN, M. A. CHEDEKEL, *The State of New York, Office of Drug Abuse Services, Testing and Research Laboratory, Brooklyn, New York, 11217, U.S.A.*

The procedure which follows is the modification of a method described by Dahlstrom & Paalzow (1975) for derivatization of morphine and codeine after extraction from biological materials.

A solution containing a small quantity of free base, 1·0 ng to 1·0 μg, of either morphine or codeine was evaporated to dryness in 15 ml conical test tube which had been treated previously with a 5% (v/v) solution of Dri-Film SC-87 in toluene (Pierce Chemical Co., Rockford, Ill.). To the tube 100 μl of glass distilled benzene (Burdick and Jackson Chemical Co., Muskegon Mich.) and 100 μl of pentafluoropropionic anhydride (Pierce Chemical Co., Rockford, Ill.) was added. The tube was capped with a size '00' thimble type stopper (A. H. Thomas Co., Phila., Pa.) then allowed to react for 25 min at 70°.

After reaction, the solvent with the reagent was evaporated to dryness at room temperature under a stream of dry nitrogen. The sample was taken up in ethyl acetate and 1 μl, containing 5 to 1000 pg μl^{-1}, was injected into a gas chromatograph (Hewlett Packard Model 5830A) equipped with a ^{63}Ni electron capture detector. The stationary liquid phase was 3% OV-22 on 80/100 Supelcoport (Supelco, Inc., Bellefonte, Pa.) in a 6 ft × 2 mm (i.d.) glass column. The carrier gas was a 90:10 mixture of argon–methane and the flow rate was set at 40 ml min^{-1}. Analysis was carried out isothermally at an oven temperature of 215°. Under these conditions the retention times for the morphine and codeine pentafluoro derivatives were 5·33 and 9·10 min, respectively.

The derivatization was carried out with several solvents: ethyl acetate, cyclohexane, toluene, and acetonitrile. The results indicated that unlike the reaction of morphine with trifluoroacetic anhydride (Wallace, Hamilton, & others, 1974) there is no critical ratio of anhydride to solvent. In fact for neat reactions there is no apparent loss in sensitivity although a higher temperature of 110° is required. For absolute standards the lower limit of sensitivity for morphine and codeine were 2 and 20 pg, respectively. This difference in sensitivity is apparently due to the fact that morphine forms a diester (Dahlstrom & Paalzow, 1975) whereas codeine most probably forms a monoester with the derivatizing agent. In addition, codeine and nalorphine are completely resolved when chromatographed under the conditions described. The retention time for nalorphine is 7·40 min. Dahlstrom & Paalzow (1975) noted that under their conditions nalorphine and codeine were not completely resolved. These derivatives are detectable on FID, however, the sensitivity is diminished.

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Antimicrobial effects of some bis-biguanides on certain bacteria which occur in connection with acne vulgaris

IDA K. HEGNA, *Department of Microbiology, Institute of Pharmacy, University of Oslo, Blindern, Oslo 3, Norway*

It has been reported that washes and lotions which contain hexachlorophene display an *in vitro* reducing effect on *Corynebacterium acnes* and *Staphylococcus albus* (*S. epidermidis*) (Jungermann & Taber 1971, Montes & Pittillo, 1972; Cunliffe, 1973), the microorganisms most frequently isolated from acne lesions (Shehadeh & Kligman, 1963; Kirschbaum & Kligman, 1963; Hall-Smith & Marks, 1973; Cunliffe, 1973). Although chlorhexidine is commonly used as a skin disinfectant (Senior, 1973), no reports on treating acne vulgaris or the acne bacteria with chlorhexidine have been recorded.

R-NH-C(NH)NH-C(NH)-NH-$[CH_2]_6$-NH-C(NH)-NH-C(NH)-NH-R

I

Ia R = cyclohexylmethyl
Ib R = 2-norbornyl
Ic R = 1,5-dimethylhexyl
Id R = 1,3-dimethylpentyl
Ie R = 2-ethylhexyl
If R = 4-chlorophenyl

Some bis-biguanides I have been evaluated, with chlorhexidine (If) as reference compound, for their *in*