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A STABILITY-INDICATING GAS-LIQUID CHROMATOGRAPHIC METHOD FOR THE DETERMINATION OF ACETAMINOPHEN AND ASPIRIN IN SUPPOSITORIES

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ABSTRACT

A stability-indicating GLC-procedure for the determination of acetaminophen and aspirin in suppositories is described. Samples were dissolved in chloroform and absolute alcohol (4:1) and gentisic acid (internal standard) was added. Solvents were evaporated and silylation accomplished by adding BSA and BSTFA (1:1) GLC-analysis was performed using a flame ionization detector and a column of 2% OV-225 on Chromosorb W. Nitrogen was used as the carrier.

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INTRODUCTION

The advantages of acetaminophen/aspirin combinations are twofold. In the first place it is known that gastric erosions caused by oral administration of aspirin are significantly inhibited by the simultaneous administration of acetaminophen(1). A second advantage is the augmentation of unhidrolized aspirin concentrations in the blood following simultaneous oral administration of aspirin and acetaminophen(2,3).

Analytical methods for the determination of aspirin and/or salicylic acid(3-12), and acetaminophen and/or p-aminophenol(13-18) have been published. The purpose of the following experiment was to develop a fast and accurate stability-indicating gas chromatographic method for the simultaneous determination of both drugs in an acetaminophen/aspirin combination. The analysis was carried out on suppositories containing acetaminophen and aspirin in a Massa Estarinum B base. The suppositories also contained diphenhydramine HCl which did not interfere with the procedure.

MATERIALS

Instrumentation - The gas chromatograph[1] was equipped with a flame ionization detector and connected to a recorder and an integrator[2].

A 2m x 3mm i.d. glass column packed with 2% OV-225 on Chromosorb W - H.P.[3] (80 - 100 mesh) and preconditioned at 200°C for 12 hours was used. The temperatures of the injection port en detector were maintained at 175°C and that of the column at 125°C. The carrier gas was nitrogen at a flowrate of ~ 35mℓ/min.

Solutions and Reagents - A solvent mixture consisting of chloroform and absolute alcohol (4:1) was used. Both solvents were AR grade. An internal standard solution was prepared by dissolving about 900mg of gentisic acid[4] (2,5-dihydroxybenzoic acid) in 100mℓ of solvent mixture. The silylation reagent was a mixture of equal parts of BSA[5] and BSTFA[5].

PROCEDURE

Five standard solutions were prepared by dissolving about 40, 45, 50, 55 and 60mg of aspirin (B.P.) accurately weighed in 30mℓ of solvent mixture. To each solution was added accurately weighed amounts of about 90, 105, 120, 135 and 150mg of acetaminophen (B.P.) respectively and mixed until dissolved. Internal standard solution (10mℓ) was added to each standard solution which was then made up to 50mℓ with solvent mixture and mixed.

The analysis was performed on suppositories containing 120mg of acetaminophen, 50mg of aspirin and 5mg of diphenhydramine HCl. Ten suppositories were weighed and shredded. An assay solution was prepared by transferring a quantity of the mass, equivalent to the active ingredients claimed to be in one suppository, to a 50mℓ volumetric flask and dissolving it in 30mℓ of solvent mixture. To this 10mℓ of internal standard solution was added, made up to 50mℓ with solvent mixture and mixed.

Aliquots of 1mℓ of the assay as well as the standard solutions were transferred to separate test tubes and evaporated to dryness using a stream of nitrogen. Care was taken during evaporation that no droplets of water formed on the inside of the test

tubes by heating them in a heating block at 35°C. Concomitantly 300µℓ of silylation reagent was added to each test tube, which were then stoppered and shaken for two minutes on a vortex shaker. The tubes were left at room temperature (27°C) for 45 minutes to allow the reaction to take place.

Two microlitres of each assay and standard solution were injected into the gas chromatograph and the peak areas of acetaminophen, aspirin and internal standard were determined. A typical chromatogram is shown in fig. 1.

Calculations - The ratios of the peak areas of acetaminophen and aspirin to the peak area of internal standard were determined. The linear regression line for these ratios on concentration (mg/mℓ) of the standard solutions were determined for both acetaminophen and aspirin. The concentration of both drugs in the assay solution was calculated using the following equation:

$$C = \frac{y-a}{m}$$

where C = concentration (mg/mℓ) of acetaminophen or aspirin

$$y = \frac{\text{peak area of drug}}{\text{peak area of internal standard}}$$ in the standard solution and a and m are the y-intercept and slope of the linear regression line for acetaminophen and aspirin in the standard solutions respectively.

RESULTS AND DISCUSSION

The linear regression lines obtained for acetaminophen and aspirin are given in figures 2 and 3. The coefficients of determination (r^2) were 0,998 (acetaminophen) and 0,991 (aspirin). Because of the

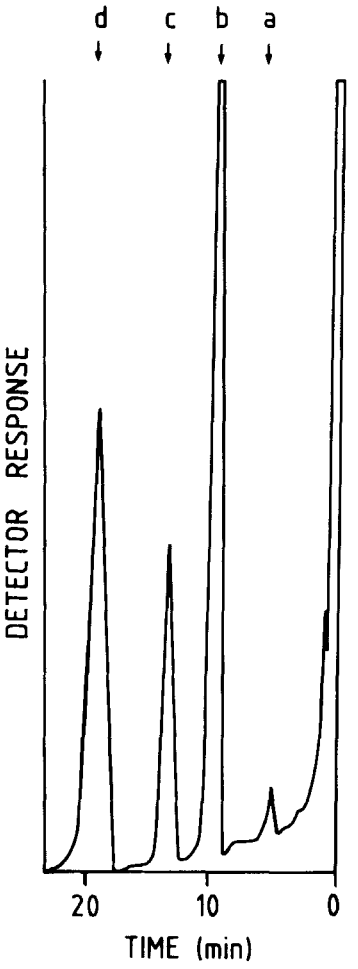

FIGURE 1

Chromatogram of a silanized sample solution containing: b,acetaminophen (2,4 mg/mℓ); c,aspirin (1 mg/mℓ); d internal standard (1,2 mg/mℓ) and traces of salicylic acid(a).

good response linearity of both drugs, their concentrations may be calculated from a single point standard.

The actual results obtained from five sample solutions are given in table 1. The coefficients of variation were 0,94% for acetaminophen and 1,50% for aspirin.

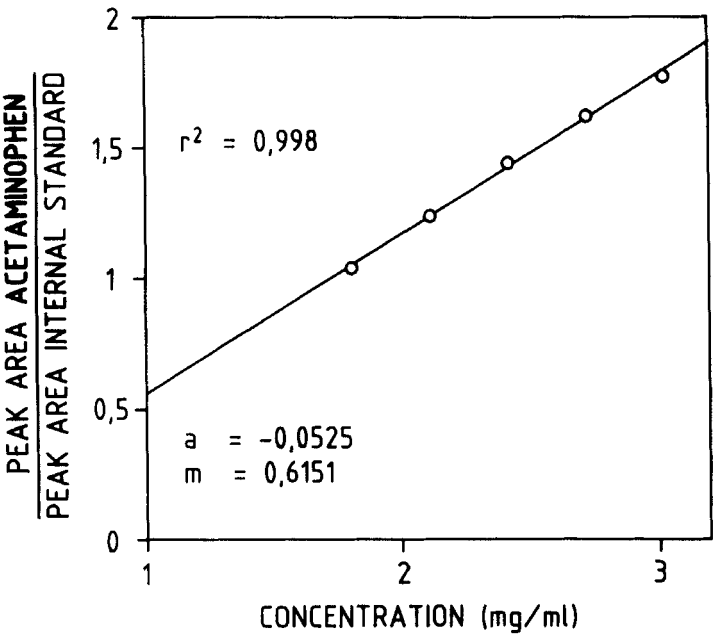

FIGURE 2

Linear regression line for acetaminophen

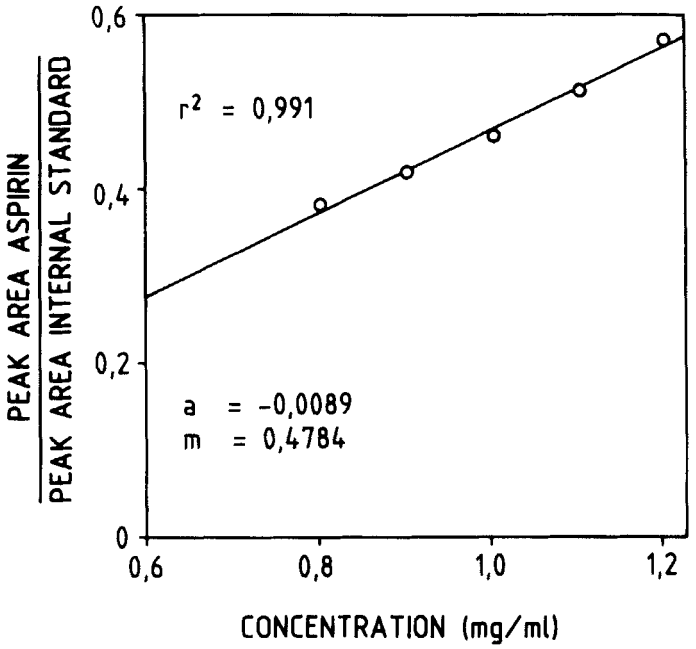

FIGURE 3

Linear regression line for aspirin

TABLE 1

Assay Results on Suppositories

Sample No	Acetaminophen % of claim	Aspirin % of claim
1	101,3	95,8
2	99,3	99,6
3	101,8	98,8
4	101,1	97,7
5	100,7	97,2
Average	100,8	97,8
Coefficient of variation	0,94%	1,50%

A solution containing acetaminophen, aspirin internal standard, degradation products (p-aminophenol and salicylic acid) and p-chloroacetanilide (contaminant) was chromatographed using the same conditions as before to establish whether the procedure was stability-indicating and to check for interference. Since the intact drugs can be measured quantitatively without interference from either degradation products or p-chloroacetanilide (fig. 4) the assay can be regarded as stability-indicating. No peaks are produced by diphenhydramine under the prescribed conditions. Propper separation of acetaminophen and aspirin could not be affected on a OV-17 column.

Although the assay was carried out on suppositories the procedure should be easily adaptable for other dosage forms.

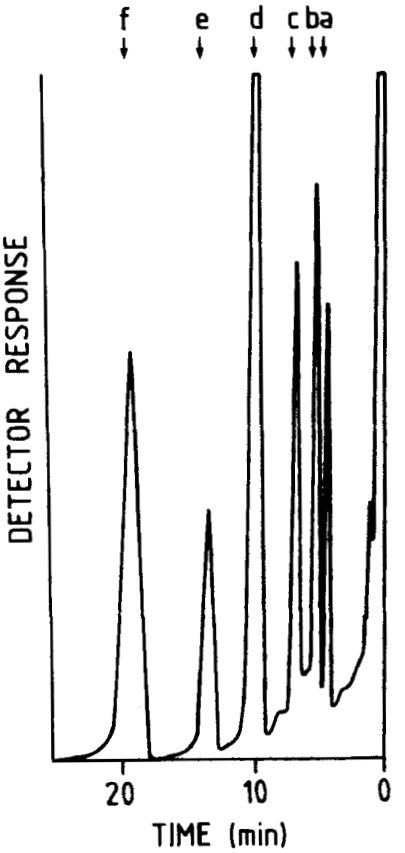

FIGURE 4

Chromatogram of a silanized sample containing: a, p-chlorocetanilide (0,6 mg/mℓ); b,salicylic acid (0,6 mg/mℓ); c,p-aminophenol (0,6 mg/mℓ); d,acetaminophen (2,4 mg/mℓ); e,aspirin (1 mg/mℓ) and f,gentisic acid (1,2 mg/mℓ)

ACKNOWLEDGMENTS

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FOOTNOTES

1 Carlo Erba, Fractovap 2150.

2 Autolab System I, Spectra Physics.

[3] Johns-Manville, Sales Corp. Supplied by Alltech Associates, Deerfield, Illinois.

[4] Merck-Schuchardt, München.

[5] Pierce Chemical Company, Rockford, Illinois.

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