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Simultaneous Determination of Salicylic Acid and Aspirin in Commercial Aspirin Tablets

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A quantitative fluorometric method was developed to determine aspirin and salicylic acid in bulk aspirin and commercial aspirin tablets. The excitation maximum for aspirin was observed at 280 nm and the emission maximum was at 335nm. The lowest energy excitation band for salicylic acid was at 308nm and the fluorescence emission band was at 450nm. Excipients, binders, lubricants and impurities did not interfere. Excellent recoveries were obtained for aspirin and salicylic acid. Results obtained by the KP III procedure and the proposed method were compared.

Key phrase: Aspirin-fluorometric determination; Salicylic acid-fluorometric determination; Fluorometric determination-analysis, aspirin and salicylic acid; Analgesics-aspirin-fluorometric determination.

Salicylates have been estimated fluorometrically. Aspirin may be estimated directly[1] or, more commonly, as salicylic acid[2,3,4]. This has been accomplished by direct hydrolysis[4] or after a separation step followed by hydrolysis[5,6,7,8].

In developing a fluorometric determination for salicylic acid in aspirin tablets, it was found that aspirin apparently fluorescenced although with much less intensity than salicylic acid[1]. This led us to measure the excitation and emission spectra of salicylic acid in aspirin tablets. Thus, we determined aspirin and salicylic acid in commercial aspirin tablets simultaneously by using the fluorometer.

Experimental

Materials—Aspirin powder(Hanil Pharm., Co.), salicylic acid(Merck Co.), EP

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grade acetic acid(Wako Co.), Spectro grade chloroform(Matheson Coleman & Bell), and Quinine bisulfate(Sigma Chem. Co.) were used. Four different brand of aspirin tablets and one brand of baby aspirin tablets were purchased from commercial sources.

Apparatus—The Baird-Atomic Fluoricord equipped with a 150 watt xenon source and quartz cuvettes(10.0mm i.d.) were used to obtain the fluorescence excitation and emission spectra. Mechanical shaker (Dong-Yang Machine Co.) was used.

Analytical Procedure—The aspirin from Hanil Pharm. Co. contained less than 2% of salicylic acid as shown by spectrophotofluorometric assay was recrystallized from benzene three times prior to use. The trace of salicylic acid in recrystallized aspirin has not been detected by spectrophotofluorometric assay. Spectroquality grade chloroform was used to make up a 1% acetic acid in chloroform solvent. Hydrolysis of aspirin can be avoided or greatly retarded by using spectroquality chloroform rather than water-washed and dried chloroform.

One hundred milligrams of recrystallized aspirin were measured accurately and dissolved in 100m*l* of acetic acid-chloroform. This solution was diluted with same solvent to make several solutions containing the aspirin at the concentration of 10,20, 30,40,50,60,70,80,100μg/m*l*, respectively.

The concentration of aspirin in each solutions was measured by spectrophotofluorometer. The fluorescence of aspirin was determined by activating at a wavelength of 280 nm and reading the emission at a wavelength of 335 nm. The calibration curve was constructed with the result of reading.

One hundred milligrams of salicylic acid were measured accurately and dissolved in 100ml of acetic acid-chloroform. Salicylic acid solution was diluted with same solvent to make the solutions containing the salicylic acid at the concentration of 0.2, 0.4, 0.6, 0.8, 1.2, 1.6, 2.0μg/m*l*, respectively.

The fluorescence of salicylic acid was measured by activating at a wavelength of 308nm and reading the emission at a wavelength of 450nm. Reading the fluorescence of each solutions results in the construction of calibration curve.

Each weight of 20 tablets of commercial aspirin containing about 500mg of aspirin per tablet, and each weight of 20 tablets of baby aspirin containing 100mg of aspirin per tablet were measured respectively. The analysis of commercial aspirin tablets and baby aspirin tablets were performed by grinding 20 tablets to a fine powder, weighing a portion of the powder equivalent to approximately 1 tablet, and placing the portion in a 100ml volumetric flask, respectively. A solvent of 1% (v/v) acetic acid in chloroform was used to dissolve the meterial and to bring the flask to volume. The solution was filtered through filter paper. One milliliter of each filtered solution was diluted to be equivalent to 40 μg/m*l* theoretically.

These solutions were examined directly on the spectrophotofluorometer for aspirin and salicylic acid simultaneously. 0.4μg/m*l* of quinine bisulfate solution was used as a reference standard to control the quantum efficiency of the fluorescence of aspirin and salicylic acid.

Results and Discussion

The simultaneous analysis of aspirin and salicylic acid was performed in a straight forward manner with minimal sample manipulation and commercially available equipment.

Figure 1 shows the uncorrected fluorescence excitation and emission spectra of aspirin in acetic acid-chloroform solution. The excitation maximum for aspirin is observed at 280 nm and the emission maximum is at 335nm. Since aspirin tends to hydrolyze to salicylic acid, it was examined the possibility that the fluorescence did not come from the aspirin but from the salicylic acid present as an impurity in the aspirin or as a hydrolyzed product of the aspirin.

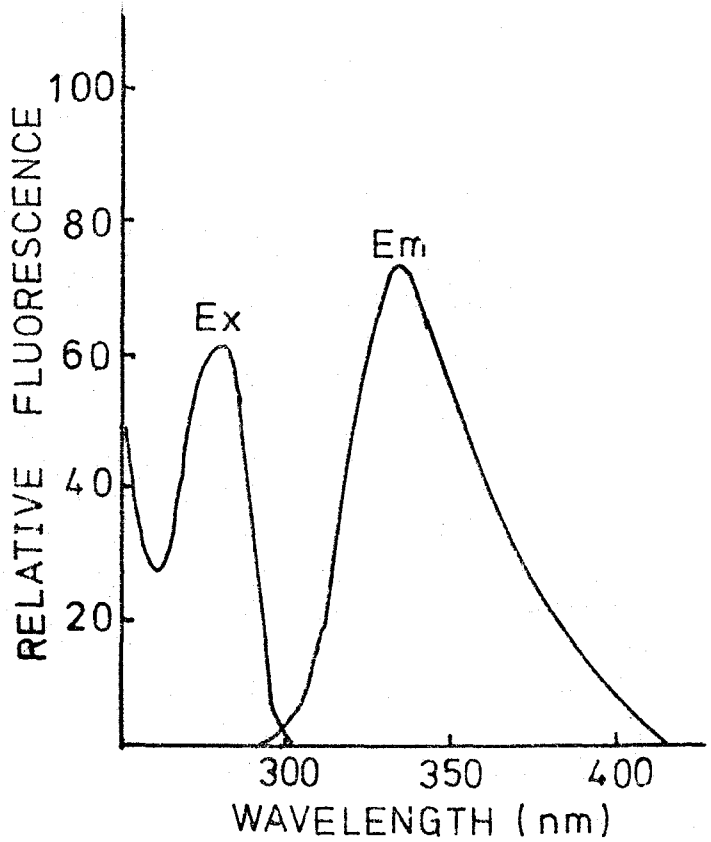

Figure 1—Excitation and emission spectra of 1.0×10^{-4}M aspirin in 1%(v/v) acetic acid in chloroform.

Figure 2 indicates the uncorrected fluorescence excitation and emission spectra of salicylic acid in the same solvent. Figure 1 and Figure 2 reveal distinct differences. The lowest energy excitation band for salicylic acid is at 308 nm and the fluorescence

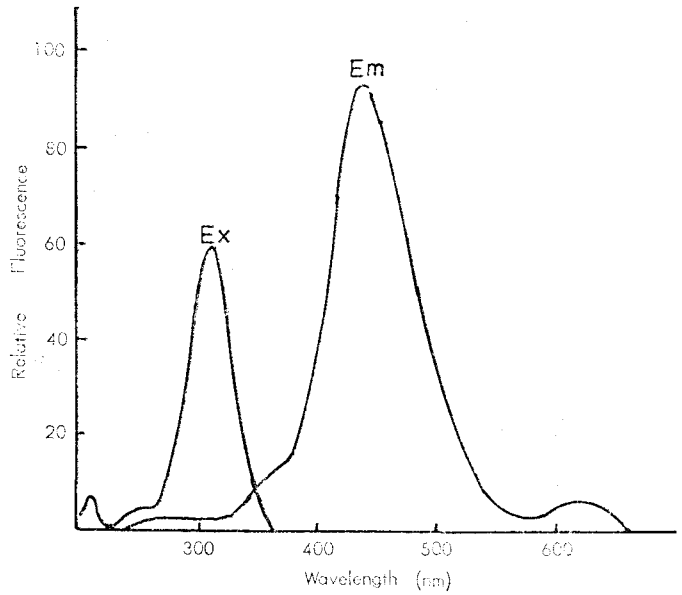

Figure 2—Excitation and emission spectra of 1.27×10^{-5}M salicylic acid in 1%(v/v) acetic acid in chloroform.

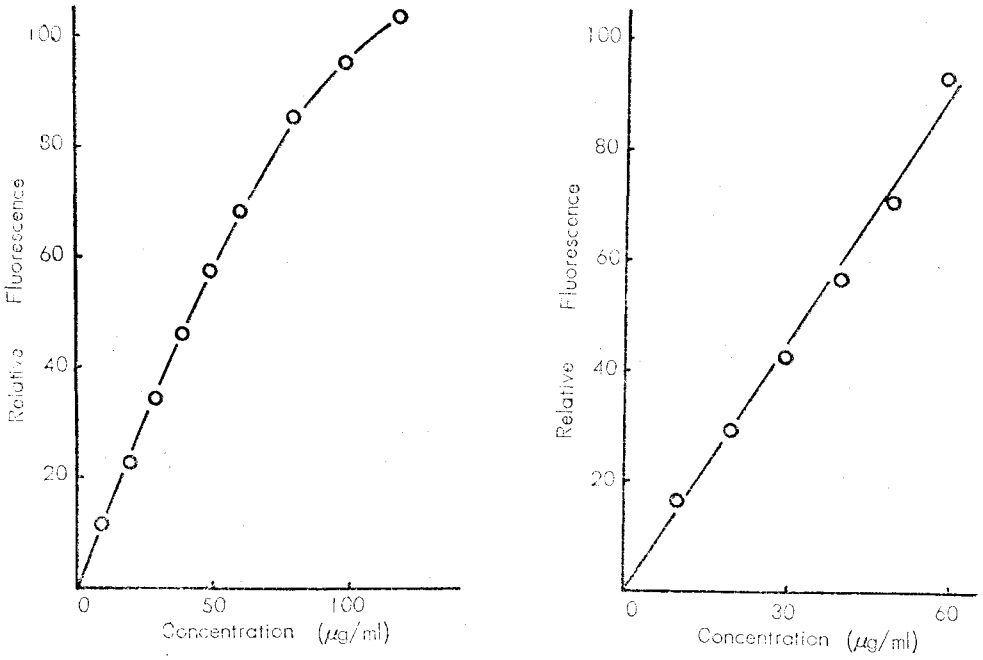

Figure 3—Linearity plot of aspirin in 1%(v/v) acetic acid in chloroform.

emission band is at 450nm. The 450nm band is much broader than that of aspirin. Thus this spectrum indicates that the fluorometric analysis of aspirin formulations for aspirin and salicylic acid appears to be feasible.

Figure 3 shows the relationship between the intensity of fluorescence emission

and the concentration of aspirin in acetic acid-chloroform solution. The calibration curve is linear over the range of 0—60μg/ml.

Figure 4 is the calibration curve of salicylic acid in acetic acid-chloroform solution. The plot is linear over the range of 0—7μg/ml. Above both concentration range, inner filtration effect and/or quenching are apparently causing some deviation from linearity.

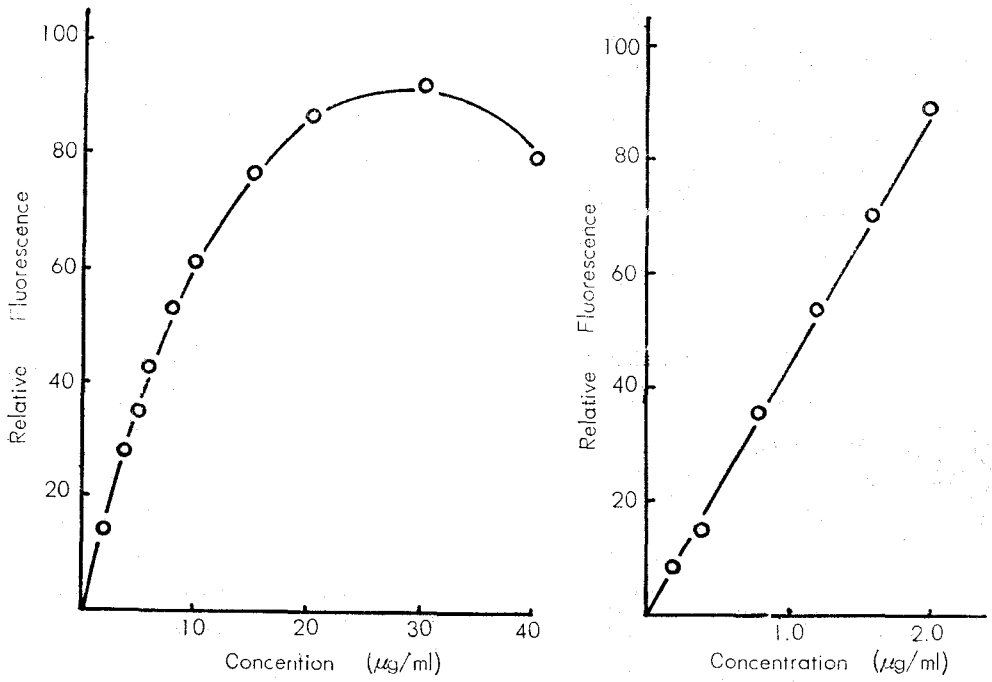

Figure 4—Linearity plot of salicylic acid in 1%(v/v) acetic acid in chloroform.

Table I—Recovery(Percent) of Salicylic Acid from Aspirin by the Proposed Method

Conc. of Aspirin Containing 1.7% Salicylic Acid(μg/ml)	Conc. of Salicylic Acid Recovered(μg/ml)	% of Salicylic Acid Recovered
10	0.15	85
20	0.36	102.85
30	0.57	108.57
40	0.69	98.57
50	0.9	102.85
60	1.08	102.85

To verify the analytical utility of the fluorescence emission of aspirin, dispensing aspirin powder containing 1.75% of salicylic acid was dissolved and analyzed by the method described in the analytical procedure. The results for salicylic acid are presented in Table I. The percentage of salicylic acid recovered in this method is much

TableII--Amounts of Aspirin and Salicylic Acid in Tablets

Drugs	Manufacturer	Manufacturing date	Tablet Dosage(mg)	Proposed Procedure		K.P. Procedure	
				Aspirin (mg)	Salicylic Acid (mg)	Aspirin (mg)	Salicylic Acid (mg)
Aspirin	A	1977. 4	500	499.33	1.18	496.23	1.19
	B	1978.10	500	491.1	1.95	493.1	1.97
	C	1976.7	250	168.48	6.9	167.7	7.1
	D	1978.12	500	498.5	1.5	492.2	1.4
Baby Aspirin	A	1978.4	100	99.8	0.17	98.3	0.12

consistent. This result indicates that fluorometric analysis of aspirin powder for aspirin and salicylic acid appears to be feasible.

The samples listed in Table II were analyzed by the method described in analytical procedure and KP III procedure. Sample A. B and D were sealed in unit dose aluminum strip package. Sample C is kept in multiple dose bottles, which is exposed to ambient air.

The precision of the proposed procedure was checked by making single determination from 10 replicate weighings of a commercial 500mg aspirin formulation from manufacturing B. The average percent of the label declaration obtained using the proposed method was 98.4% for aspirin and 0.39% for salicylic acid, respectively. The average of duplicate determination of aspirin and salicylic acid using the KP III procedure were 97.8% for aspirin and 0.39% for salicylic acid, respectively.

The method presented here is reliable and relatively free from excipient interference. The equipment is commercially available and easy to assess. In addition, the determination of salicylic acid and aspirin can be accomplished simultaneously without separation of salicylic acid and aspirin. The amount of interference of salicylic acid with aspirin will be negligible for most formulations. If salicylic acid levels are high, the aspirin analysis also can be corrected. This method is applicable to all dosage levels and sensitive enough for content uniformity determination, or monitoring stability of aspirin tablets in the market.

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