Simultaneous Spectrofluorometric Determination of Aspirin and Salicylic Acid in Aqueous Solution

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The fluorescence of aspirin in solution and a quantitative assay in the presence of salicylic acid was first reported by Miles and Schenk (1). A solvent of 1 % acetic acid in chloroform was chosen in that study, because it gave appropriate separation of the fluorescent emission maxima of aspirin and salicylic acid whereas isopropanol did not. Since salicylic acid is a degradation product of aspirin, others have measured salicylic acid in preparations containing aspirin as well as other substances without interference employing spectrofluorimetry (2, 3). More recently, fluorescence detection employing high pressure liquid chromatography has been reported for the simultaneous determination of aspirin and salicylic acid (4).

In an attempt to develop a sensitive spectrofluorometric assay of aspirin and salicylic acid in an aqueous phospholipid system, it was discovered that a simultaneous determination of aspirin and salicylic acid in aqueous acidic solution was possible, being rapid, convenient, and sufficiently sensitive. Standard solutions used to construct calibration curves of aspirin and salicylic acid were prepared in acidic buffer solution (0.004 moles HCl + 0.016 moles KCl per 100 ml water, HCl-KCl solution, pH 2.0) containing either the pure compound or various ratios of aspirin to salicylic acid. Typically, 200 mg aspirin were initially dissolved in 25 ml ethanol, then made up to 100 ml with HCl-KCl buffer solution. Similarly, 100 mg salicylic acid were dissolved in 100 ml HCl-KCl solution. Each was then further diluted 1 in 20 to yield the final stock solutions. Subsequently, various aliquots of these stock solutions were combined in a 50 ml flask and made to volume with HCl-KCl solution to obtain the solutions for calibration. Fluorescence measurements were made on an Aminco-Bowman Spectrofluorometer (J4-8202) at room temperature. Samples were placed in 1 cm quartz cells and excitation and emission spectra determined. The excitation and emission maxima for aspirin in aqueous acidic solution were 275 nm and 350 nm, respectively (cf. 280 nm and 335 nm, respectively in 1 % acetic acid in chloroform (1)). Similarly, the excitation and emission maxima for salicylic acid were 295 nm and 415 nm, respectively (cf. 308 nm and 450 nm in 1 % acetic acid in chloroform (1)). A second smaller emission peak appeared at lower wavelengths in each spectrum, presumably due to a buffer component, but it had no effect on the emission spectrum of either compound. Furthermore, there was no interference by salicylic acid on the fluorescence intensity of aspirin, and vice versa, when both were present in the same solution. The same calibration curves were obtained when measuring solutions of the compounds individually or in combination. The calibration curve for aspirin is linear in a plot of fluorescence intensity versus concentration over the range 2–10 μg/ml ($y = 5.62\,x + 0.33$, $r = 1.00$). The calibration curve for salicylic acid is linear over the range 1–4 μg/ml ($y = 11.24x + 1.2$, $r = 0.999$). Above this concentration there is negative deviation from linearity in agreement with previous reports (5). The reason for this is probably self-quenching which is more pronounced for salicylic acid than aspirin (6). The sensitivity of the analysis for aspirin is approximately 1 μg/ml and about 0.5 μg/ml for salicylic acid.

Tests of the analytical utility of fluorescence emission in aqueous buffer solution were conducted by measuring the aspirin content of commercial tablets (Entrophen tablets, 325 mg) and the kinetics of degradation of aspirin in solution. Twenty tablets were ground to a fine powder using a mortar and pestle. A portion of the powder equivalent to the weight of a tablet was weighed and dissolved in 25 ml ethanol and diluted to 100 ml with HCl-KCl solution. The solution was filtered, then 1 ml of the filtrate was diluted to 50 ml followed by a further dilution of 4 ml to 25 ml with HCl-KCl. This solution was then analyzed directly against an HCl-KCl reference solution. The result obtained with these different samples was 324.1 ± 3.2 mg per tablet. In addition, the method was sufficiently sensitive to detect 0.28 ± 0.03 mg salicylic acid present per tablet (~ 0.1 %).

Secondly, the degradation kinetics of 5.55×10^{-5} M aspirin at pH 2.0 and 20°C were measured. Both aspirin concentration remaining and salicylic acid concentration formed at various time intervals were conveniently measured yielding the first-order plot shown in Fig. 1 from which the rate constant of degradation was calculated to be 0.0528 day^{-1} ($r = 0.994$)) which compares with 0.0456 day^{-1} at 17° C (7). The sum of the aspirin concentrations remaining and

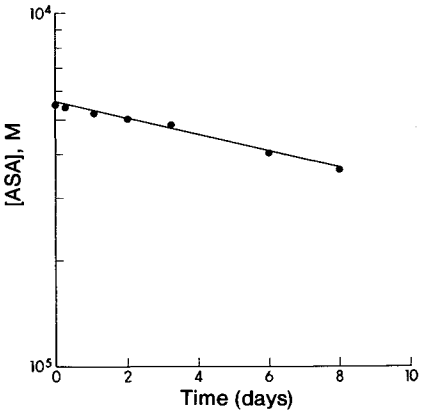

Fig. 1 Degradation of aspirin determined by spectrofluorometric analysis in pH 2.0 buffer solution λ (excitation) = 275 nm; λ (emission) = 350 nm. There is no interference by salicylic acid for which λ (excitation) = 295 nm; λ (emission) = 415 nm.

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the salicylic acid concentrations formed at each interval over an eight day period was 99.2 ± 2.7 %.

Spectrofluorometric analysis is a sensitive method of analysis for many compounds, particularly aspirin. One of the drawbacks has been the perceived necessity for several extractions into organic solvents prior to analysis. It has now been shown that for aspirin and salicylic acid determination in the same preparation, such as may be required in tests of strength, dissolution or degradation rate, it is convenient to employ spectrofluorometric analysis in aqueous buffer solution. At pH 2.0 there is negligible degradation of aspirin during sample preparation.

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