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LETTER TO THE EDITOR

DEGRADATION OF ASPIRIN IN SOLUTIONS

To The Editor:

One of the major tenets of any method of analysis in the scientific or non-scientific world, is that the method of analysis should not affect the sample. Many authors have published methods for aspirin, salicylic acid and other components in pharmaceutical preparations, and one of their major concerns was that the aspirin should not degrade to salicylic acid in the sample solution. This was also an important consideration during the development and implementation of the USP assay for aspirin tablets in the period 1982-1984[1-3]. We were able to participate in the development of the USP monograph[3]. We did not develop the original method but during our evaluation we showed that there was no significant degradation of the aspirin to salicylic acid in the sample solution in a 22 hour period.

We were therefore surprised to see the recent paper by Yang et al[4] which did not address the stability of aspirin in the described sample solutions although the paper notes the instability of aspirin and its ready hydrolysis to salicylic acid. Consequently we prepared solutions of aspirin in 10% ethanol as described by Yang[4] and also in acetonitrile/1% formic acid as used in the USP method we developed for butalbital and aspirin tablets[5]. We assayed the two solutions for free salicylic acid as a % of the initial aspirin concentration by the USP method for butalbital and aspirin tablets[5]. The results are given in Table I.

TABLE I

Stability of Aspirin Solutions

% Salicylic acid as % of initial aspirin concentration

Time (hrs)	Aspirin in 10% ethanol/90% water	Aspirin in 99% Acetonitrile/ 1% Formic acid
Initial	0.20*	ND**
4	1.80	ND**
8	3.47	0.06
12	5.13	0.06
16	6.69	0.09
20	8.34	0.10
24	9.85	0.09
28	11.1	0.13
32	12.4	0.13
36	13.5	0.17
40	14.9	0.18

*Assayed within 30 minutes of preparation

**None detected

As can be seen from the results, the aspirin rapidly degrades in the aqueous ethanol solution such that within 8 hours, over 3% of salicylic acid has been formed. This precludes the use of an autosampler for the assay as results obtained on an 8 hour old sample solution would cause the sample to fail to meet the USP specification of not more than 3% free salicylic acid in coated aspirin tablets or those containing buffers. This is a typical limit for aspirin combination tablets.

The separation of aspirin, caffeine, dihydrocodeine bitartrate, promethazine HCl, salicylic acid and acetanilide (IS) is

impressive. However we would like to suggest that the standards (at least the aspirin standard) and the samples be prepared in a solvent mixture such as acetonitrile/1% formic acid, in which insignificant hydrolysis of the aspirin will occur during the analysis.

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