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Short Communication

The analysis of pharmaceutical preparations using solid-surface room temperature photochemical-fluorescence*

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Introduction

Manufacturers use a variety of additives in pharmaceutical preparations in order to increase their stability or to facilitate the biological absorption of the drugs. Specific methods of analysis are required for the quality control of active ingredients in dosage forms containing additives. However, in many cases the current official procedures for determining drugs in pharmaceutical preparations are rather tedious and cumbersome [1]. As a consequence, high-performance liquid chromatography (HPLC) and thin-layer chromatography [2, 3], as well as luminescence methods [4, 5] are frequently used for the quality control assay of pharmaceutical formulations, because of their excellent selectivity and sensitivity.

Recently, room temperature photochemical-fluorescence (RTPF) has been demonstrated to be a versatile, selective, and sensitive analytical method for assaying a variety of photochemically active organic compounds [6–28]. RTPF is also a very adaptable technique, as it has been used in several experimental modes, such as in liquid bulk solutions [7–13, 28], HPLC [14–22], flow injection analysis [23, 24], and on solid surfaces [25–28]. However, only a few applications of the technique have been described, for the analysis of drugs and metabolites in serum and other biological fluids [14, 16, 17, 19, 23, 24].

In the present paper the usefulness of solid-surface room temperature photochemical-fluorescence (SS–RTPF) for the quantitative analysis of several drugs in pharmaceutical preparations is evaluated.

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Experimental

Reagents

All pharmaceutical preparations (Table 1) were purchased from local pharmacies. Reference compounds were obtained from Aldrich Chemical Co. (acetylsalicylic acid), Sigma Chemical Co. (chloroquine phosphate), and United States Biochemical Corp. (theophylline).

Apparatus

A Turner model 111 filter fluorimeter and a Kontron model SF M-125 spectrophotofluorimeter were used for the fluorescence measurements. A 200-W Osram mercury arc lamp with an Oriel model 8500 power supply was used for the photolysis.

Standard and sample solutions

Standard solutions of the reference compounds were prepared by the serial dilution of neutral or alkaline (pH = 10.0) aqueous stock solutions (1000 μg/ml). For the analysis of pharmaceutical formulations (Table 1) samples were prepared by the dissolution of tablets or capsule contents with water or 0.1 mM sodium hydroxide aqueous solution. One tablet or the contents of one capsule was dissolved in 10–500 ml of the appropriate solvent and then further diluted to give sample solutions of nominal concentration between 70 and 200 μg/ml.

Procedure

A laboratory-constructed aluminium sample holder [29] and filter paper discs were used for fluorescence measurements. Several filter papers were tested for their fluorescence background signal and the sample fluorescence intensity (Table 2).

Whatman No. 1 filter paper was chosen as the optimum solid substrate, as it gave the largest analyte fluorescence intensity and the lowest background signal. 5-μl samples were spotted on to the paper discs, with a Hamilton 10-μl microsyringe. The samples were dried for 10 min in a hot-air current. Two procedures were used for photochemical-fluorescence measurements. In the first procedure the sample holder was placed at about 60 cm from the mercury arc lamp and irradiated for a fixed period of time, then immediately transferred to the Turner fluorimeter sample compartment for measuring the fluorescence intensity of the spots. In the second procedure irradiation *in situ* and fluorescence measurement were performed simultaneously using the Kontron spectrophotofluorimeter. Fluorescence signal versus irradiation time $f(I_F, t_{irr.}) = O$ curves were recorded directly for a period of about 5 min for the standard and sample solutions spotted onto filter paper. Calibration curves were established using the integrated photochemical-fluorescence intensities of standard solutions of the reference compounds. The range of linearity was determined and linear regression analysis of data was performed on a programmable pocket calculater. Quantitation was carried out by comparing the relative fluorescence intensities of the sample solutions to those of the standard solutions using the linear regression data (Table 3).

Results and Discussion

The results of the assays of acetylsalicylic acid, chloroquine and theophylline in various pharmaceutical formulations, including tablets, powders and syrups are shown in Table

Table 1
Assay of pharmaceutical preparations

Formulation	Source	Active ingredient	Stated content* (mg)	Content of ingredient found†	Mean range
Alka-Seltzer (tablets)	Miles	Acetylsalicylic acid	320	105	99–109
Armophylline (tablets)	Armour–Montaga	Theophylline	50	116	110–122
Aspegic (powder)	Egic	Acetylsalicylic acid	250	109	104–114
Aspegic (powder)	Egic	Acetylsalicylic acid	500	109	103–113
Catalgine (powder)	Theraplix	Acetylsalicylic acid	100	110	105–115
Catalgine (powder)	Theraplix	Acetylsalicylic acid	250	109	104–114
Catalgine (powder)	Theraplix	Acetylsalicylic acid	500	110	105–115
Chloroquine 100 (tablets)	Sipoa	Chloroquine	100	108	103–113
Nivaquine (tablets)	Specia	Chloroquine	100	108	103–113
Theolair L.A. (tablets)	Riker	Theophylline	175	107	102–112
Theophylline (syrup)	Bruneau	Theophylline	240	98	93–103

*Active ingredient expressed in mg per dosage form.
†Expressed as percentage recovery relative to stated content.

Table 2
Comparison of the background and standard fluorescence signals determined on several filter papers

Filter	Background signal*	Net I_F†	
		Salicylic acid	Chloroquine
S & S 904	15	9.5	26
Whatman No. 1	11	13.5	28
Whatman No. 41	12	11.5	26
DE-81	12.5	10	23

*Relative to the fluorescence intensity (I_F = 10) of a 7.25×10^{-4}M solution of salicylic acid spotted on to DE-81 filter paper.
†Net fluorescence intensity, corrected for background fluorescence intensity and relative to the I_F (10) of a 7.25×10^{-4}M solution of salicylic acid spotted on to DE-81 filter paper.

Table 3
Statistical treatment of the photochemical fluorimetric calibration curves

Compound	Analytical wavelength $\lambda_{ex}/\lambda_{em}$ (nm)	Linear dynamic range (μg/ml)	Regression data‡	Correlation coefficient
Acetylsalicylic acid*	305/408	20–200	$y = 0.66x + 0.12$	0.999
Chloroquine†	340/375	20–1000	$y = 0.56x - 0.32$	0.992
Theophylline*	272/315	20–200	$y = 0.43x + 0.77$	0.982

*In alkaline (pH = 10.0) aqueous solution.
†In neutral (pH = 7.0) aqueous solution.
‡y = Integrated fluorescence intensities and x = concentration of solution (in μg ml^{-1}) spotted on to filter paper.

1. With the exception of Armophylline satisfactory recoveries were obtained, although, for some formulations the results were slightly larger than those permitted by USP formulation analysis guidelines (90–110% content of the active ingredient). Precision studies with 4–6 determinations of each sample and standard solution gave relative standard deviation values between 4 and 5%. No compound other than the active ingredients appeared to fluoresce significantly showing that various formulation matrices can be analysed by SS–RTPF with no significant interference due to background fluorescence.

Solid-surface room temperature photochemical-fluorescence is worthy of consideration as a simple, inexpensive, and selective analytical technique for the quality control assay of certain active ingredients in pharmaceutical formulations.

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