Pak. j. sci. ind. res., vol. 32, no. 3, March 1989

QUANTITATIVE INFRARED DETERMINATION OF SOME ACTIVE CONSTITUENTS OF DRUGS

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(Received December 28, 1986; revised February 23, 1989)

An infrared method involving the use of base line technique for the assay of aspirin, nicotinamide, meprobamate and salicylamide in neat solutions, pharmaceutical products and laboratory prepared multicomponent mixtures has been described. Method is simple, rapid and shows good results. Assay of authentic samples and pharmaceutical products has shown percentage error of 1-2 %. However, the assay of multicomponent mixtures has shown results of moderate accuracy.

Key words: Infrared, Aspirin, Nicotinamide.

INTRODUCTION

Infrared spectroscopy for quantitative analysis of the active constituents of pharmaceutical preparation was introduced by Washburn *et. al.* [1]. Subsequently this technique has been used by a number of workers [2-10] for the quantitative determination of the active constituents of pharmaceutical products and in the assay of geometrical isomers [11]. In the present work a quantitative determination of active constituents (i.e. aspirin, nicotinamide, meprobamate and salicylamide) using their various distinguishing peaks has been carried out in neat solutions, pharmaceutical products and laboratory prepared multiple-component mixtures.

EXPERIMENTAL

Reagents. (a) Chloroform (A.R. grade BDH). Traces of moisture and alcohol were removed by first extracting the alcohol from chloroform (30ml) with water (50x3ml) and then eliminating the water by passing through a glass column (500x30 m m) containing activated alumina.

(b) Aspirin (Acetylsalicylic acid), meprobamate, salicylamide and nicotinamide used were of analytical grade.

Preparation of standard solutions. Standard solutions of aspirin, meprobamate salicylamide and nicotinamide were prepared by dissolving 50.00, 100.00, 150.00, 200.00 mg of each in 10 ml of the chloroform to get 0.5 %, 1.00 %, 1.5 % and 2 % solution of each compound respectively.

Preparation of sample solutions. A portion of finely pulverized tablets of pharmaceutical product was accurately weighed containing not more than 100 mg of the active constituents and extracted 5 times with one ml. portion of dry and ethanol free chloroform, then volume made upto 10 ml. and finally filtered through Whatman No. 1 paper. The filtrate was used for the assay of active constituents. The solutions of the mixtures of the pharmaceutical products were also prepared by the same procedure.

Apparatus. Spectrophotometer- JASCO Model IRA-1 with sodium chloride cell of thickness 0.5mm, and wave number range 4000-650 cm^{-1} was used. Scanning time of 32 minutes was used for better resolution of characteristic absorption peaks.

General procedure and calculation. Exactly 1ml of the standard solution was introduced in the cell with the help of a microsyringe. The spectra were recorded for the solution against a reference blank containing the solvent only (i.e. chloroform). The absorbance (A) was calculated from the specific absorption peaks of aspirin (1600, 900 cm^{-1}), meprobamate (1576, 3500 cm^{-1}), salcylamide (1360, 3500 cm^{-1}) and nicotinamide (1578, 3400 cm^{-1}) for standard solutions.

The absorption spectra for the sample solutions of the pharmaceutical products and multicomponent mixtures were also measured as described for the standard solutions using chloroform as a solvent.

Results were calculated using the base-line method [12] and the following relationship.

$$C = \frac{A}{a\ b\ c'}$$

- A = Absorption of a particular component in the sample.
- a = Absorptivity (determined with a known concentration of the particular pure component).
- b = Cell thickness in mm.
- c' = Concentration of the sample (active component plus adulterants) in the analytical solution.
- C = Concentration of the desired constituent in the sample.

(Beer's law was applied in Infrared determinations just as it is applied in visible or ultraviolet spectrophotometric determinations).

DISCUSSION

A series of standard solutions (0.5 to 2.0 %) of pure aspirin, meprobamate, salicylamide and nicotinamide were analysed using the absorption peaks at 1600, 900 cm^{-1}; 1576, 2500 cm^{-1}; 1360, 3500 cm^{-1} and 1578, 3400 cm^{-1} respectively. These peaks were choosen beacause experimentation showed that these were associated with least interferences. Adherence to Beer's law [13] was observed at these maxima over a wide range of concentration (0.5 to 2 %). Assay of authentic (pure) samples of these compounds at these maxima showed an error of 1-2 % (Table 1). Three determinations were carried out of each sample for each maxima. In the assay of meprobamate, salicylamide and nicotinamide in the region 3400-3500 cm^{-1}, the alcohol present as preservative and traces of water must be removed from the chloroform used as solvent in order to avoid their interference in the assay of these constituents.

In addition, the data pertaining to the assay of aspirin, meprobamate, salicylamide and nicotinamide in pharmaceutical products are collected in Table 2. Estimation of aspirin using the peak at 1600 cm^{-1} (due to –c=C–) showed a percentage error of 1-2 % for sample No. 1–4. However, the use of peak at 900 cm^{-1} (due to out of plane

Table 1. Results of analysis of pure samples of aspirin, meprobamate, salicylamide and nicotinamide.

Sample amount present mg %	Aspirin (mg%) 1600 cm^{-1} Found*	Error %	900 cm^{-1} Found*	Error %	Meprobamate (mg%) 1576 cm^{-1} Found*	Error %	3500 cm^{-1} Found*	Error %	Salicylamide (mg%) 1360 cm^{-1} Found*	Error %	3500 cm^{-1} Found*	Error %	Nicotinamide (mg%) 1578 cm^{-1} Found*	Error %	3400 cm^{-1} Found*	Error %
90.00	89.50	– 0.5	89.2	– 0.80	91.00	+ 1.00	91.5	+ 1.50	88.0	– 2.00	88.50	– 1.50	90.20	+ 0.20	89.00	– 1.00
60.00	60.00	0.0	59.2	– 0.8	59.00.	– 1.00	61.0	+ 1.00	58.9	– 1.10	59.2	– 0.80	60.10	+ 0.10	59.00	– 1.00
40.00	39.6	– 0.4	39.4	– 0.6	39.2	– 0.80	42.0	+ 2.00	41.0	+ 1.00	38.1	– 1.90	41.20	+ 1.20	38.2	– 1.8
25.00	24.80	– 0.2	25.1	+ 0.10	24.8	– 0.20	26.1	+ 1.1	26.5	+ 1.50	25.4	+ 0.40	25.3	+ 25.3	24.00	– 1.00

*Average of three determinations.

Table 2. Estimation of aspirin, meprobamate, salicylamide and nicotinamide in pharmaceutical products.

Sample	Contents of sample solution (mg %)	Found* mg % (w/w) Aspirin 1600 cm^{-1}	Aspirin 900 cm^{-1}	Meprobamate 1576 cm^{-1}	Meprobamate 3500 cm^{-1}	Salicylamide 3500 cm^{-1}	Nicotinamide 1578 cm^{-1}	Nicotinamide 3400 cm^{-1}	% Error
Aspirin tab.	Aspirin=100	101.1	97.5	–	–	–	–	+ 1.11	– 2.5
Parapyrin tab.	Aspirin=100	101.5	93.5	–	–	–	–	+ 1.5	– 6.5
Emprin-S tab.	Aspirin=100	102.0	94.0	–	–	–	–	+ 2.0	– 6.0
Emprin compound tab.	Aspirin=88.24 Caffeine=11.76	86.80	80.0	–	–	–	–	– 1.44	– 8.24
Equanil tab.	Meprobamate=100	–	–	95.75	98.57	–	–	– 4.25	– 1.43
Malidens	Salicylamide=90 Caffeine=0.09	–	–	–	–	87.78	–	– 2.22	–
Rapceen	Salicylamide=89.28 Caffeine=10.71	–	–	–	–	84.00	–	–	– 5.28
Stress capsule	Nicotinamide=100	–	–	–	–	–	102	107.11 +2	+ 7.11

*Average of three determinations.

Table 3. Estimation in multi-component mixtures.

Mixture (A) = Aspirin (at 900 cm^{-1}) and meprobamate (at 3500 cm^{-1}).
Mixture (B) = Aspirin (at 900 cm^{-1}) and salicylamide (at 3500 cm^{-1}).

Sample	Composition of sample solution (mg%)		Found (mg%)		Error %	
Mixture (A)	Aspirin	Meprobamate	Aspirin	Meprobamate	Aspirin	Meprobamate
1. Aspirin tab. + Equanil tab.	55	45	48.32	40.5	– 6.68	– 4.5
2. Parapyrin tab. + Equanil tab.	55	45	50.5	41.5	– 4.5	– 3.5
3. Emprin-S tab. + Equanil tab.	55	45	51.6	39.54	– 4.4	– 5.46
4. Disprin tab. + Equanil tab.	55	45	49.8	43.46	– 5.2	– 1.54
Mixture (B)	Aspirin	Salicylamide	Aspirin	Salicylamide	Aspirin	Salicylamide
1. Aspirin tab. + rapceen tab.	52.18	42.69	48.75	39.45	– 3.43	– 3.24
2. Parapyrin tab. + rapceen tab.	52.18	42.69	46.52	36.84	– 5.66	+ 5.85
3. Emprin-S tab. + rapceen tab.	52.18	42.69	48.51	46.82	– 3.67	+ 4.13
4. Disprin tab. + rapceen tab.	52.18	42.69	46.10	46.51	– 6.08	+ 3.82
5. Aspirin tab. + malidens tab.	57.69	38.46	52.51	42.21	– 5.18	+ 3.75
6. Disprin tab. + malidens tab.	47.62	47.62	43.21	52.82	– 4.41	+ 5.20
7. Emprin compound + malidens tab.	53.57	35.71	48.20	40.85	– 5.37	+ 5.14

–OH deformation) exhibited a greater percentage error (6.5-8.24) for sample No. 2-4 but reasonably good result (i.e. % error of 2.5) was obtained for sample No. 1. Estimation of meprobamate in commercial sample No. 5 using frequencies at 1576 cm^{-1} (NH-bending in NH_2 group) and at 3500 cm^{-1} (NH-stretching in primary amide) has shown a percentage error of –4.25 and –1.43 respectively. The results obtained are comparable with official NF method [14] and other reported method [10]. Using the absorption peak at 3500 cm^{-1} due to –NH stretching in primary amide, the estimation of salicylamide has shown a % error of 2.22 and 5.28 for sample No. 6 and 7 respectively. Assay of nicotinamide in commercial sample No. 8 using the frequency at 1578 cm^{-1} has shown good results (% error=2) which is comparable with previously reported [10] estimation of nicotinamide at 1700 cm^{-1}. However, a higher percentage error (+ 7.11) was observed at 3400 cm^{-1}.

The results presented in Tables 1 and 2 gave percentage error comparable to other methods, e.g. titrimetric method and HPLC method [15] (for salicylamide), hydrolysis based method [16,17] (for aspirin) and N– based method [18] (for nicotinamide). The higher error found in the pharmaceutical sample analysis (Table 2) may be ascribed to the interference from the presence of excipients. However, a number of liquid & high performance liquid chromatographic (HPLC) methods have been described for the determination of nicotinamide in biological fluids [19], pharmaceutical preparations [20,21] and beef pork [22]. The proposed HPLC methods are suitable for the determination of nicotinamide with detection limits as low as 1-2 ng. The infrared method, however, would not be expected to be as precise as the usual HPLC, titrimetric methods or on-line bromimetric determination of aspirin using flow injection voltammetry [23] carried out at lower concentrations but it is more convenient and sufficiently precise for use in certain applications.

Applicability of this method for simultaneous assay of the aspirin and meprobamate or aspirin and salicylamide or aspirin and nicotinamide in laboratory prepared mixtures was also investigated. Results (Table 3) show a moodrate accuracy for mixture (A) of aspirin – meprobamate and mixture (B) aspirin – salicylamide but the mixture of aspirin – nicotinamide did not give well resolved characteristic peaks which could be reliably used for the estimation of these compounds.

From the results obtained in the present study it may be concluded that infared method can be reliably used for the estimation of aspirin, meprobamate, nicotinamide and salicylamide in neat solutions and pharmaceutical products.

In mixture analysis as evident from the results of Table 3 the percentage error may have been reduced by incorporating separational method prior to the use of

infrared for quantitative purposes. This however, needs itself a separate study.

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