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Infrared identification of sulphonamides using attenuated total reflection

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The infrared spectra of ten sulphonamides have been determined by attenuated total reflection and compared with transmission spectra. No major differences were found in the positions and shapes of the main absorption peaks and it was possible to use ATR to identify sulphacetamide sodium in eye-drops and in eye ointments.

The ready identification of sulphonamides in the solid state by infrared absorption spectra can be complicated by the occurrence of polymorphic forms which give rise to different infrared spectra (Mesley & Houghton, 1967; Moustafa & Carless, 1969). To allow for these different forms the sample for identification and the Authentic Specimen must both be converted to the same crystalline form before spectra can be compared.

Since the introduction of attenuated total reflection (ATR) (Fahrenfort, 1961) this technique has found many applications for obtaining spectra of substances difficult or impossible to obtain by transmission (Katlafsky & Keller, 1963; Wilks, 1965; Pawlak, Fricke & Szymanski, 1967; Wilks & Hirschfeld, 1967). Its use for the identification of sulphonamides has been investigated since the ATR spectra of drugs can be rapidly determined after applying the sample in acetone solution to the reflector plate and evaporating. It was expected that, following this treatment, the same polymorphic form of the drug would always be produced. In addition, transmission and ATR spectra of the same sulphonamides in Nujol mulls were recorded for comparison. ATR spectra of sulphacetamide eye ointments and eye-drops were also examined.

MATERIALS AND METHODS

Apparatus

Infrared spectra of Nujol mulls were recorded on a Hilger H900 Infrascan spectrophotometer. For ATR spectra a Wiltek Model 9T multiple internal reflection attachment was used, with a 45° KRS-5 (thallous bromide-iodide) reflector plate (50 × 20 × 2 mm) held in a M1R-1 Teflon holder. A variable beam attenuator in the reference beam was used to balance the energy levels between sample and reference beam.

Materials

B.P. Authentic Specimens of sulphacetamide sodium, sulphadiazine, sulphadimethoxine, sulphadimidine, sulphadimidine sodium, sulphafurazole, sulphamethizole, sulphamethoxydiazine, sulphamethoxypyridazine and sulphapyridine were used. In several cases ATR spectra were obtained from commercial samples of sulphonamides for comparison. Proprietary samples of sulphacetamide eye oint-

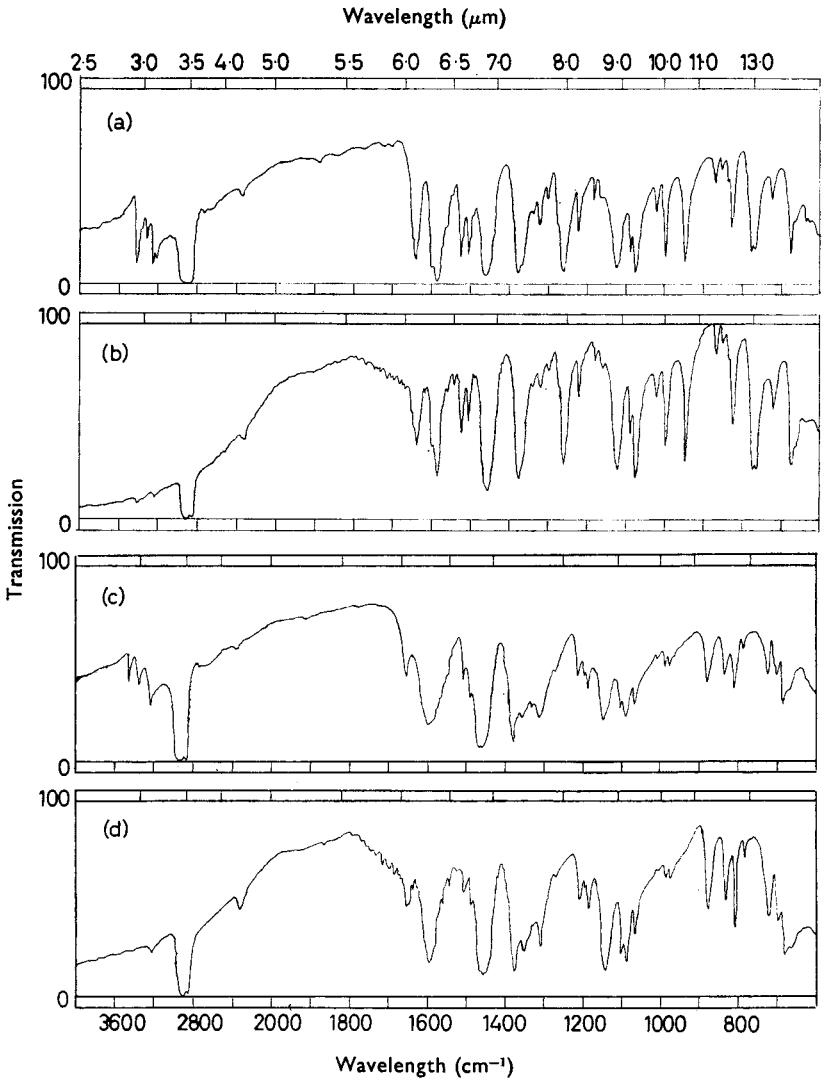

FIG. 1. Infrared spectra in Nujol mulls: (a) transmission and (b) ATR of sulphapyridine; (c) transmission and (d) ATR of sulphadimethoxine.

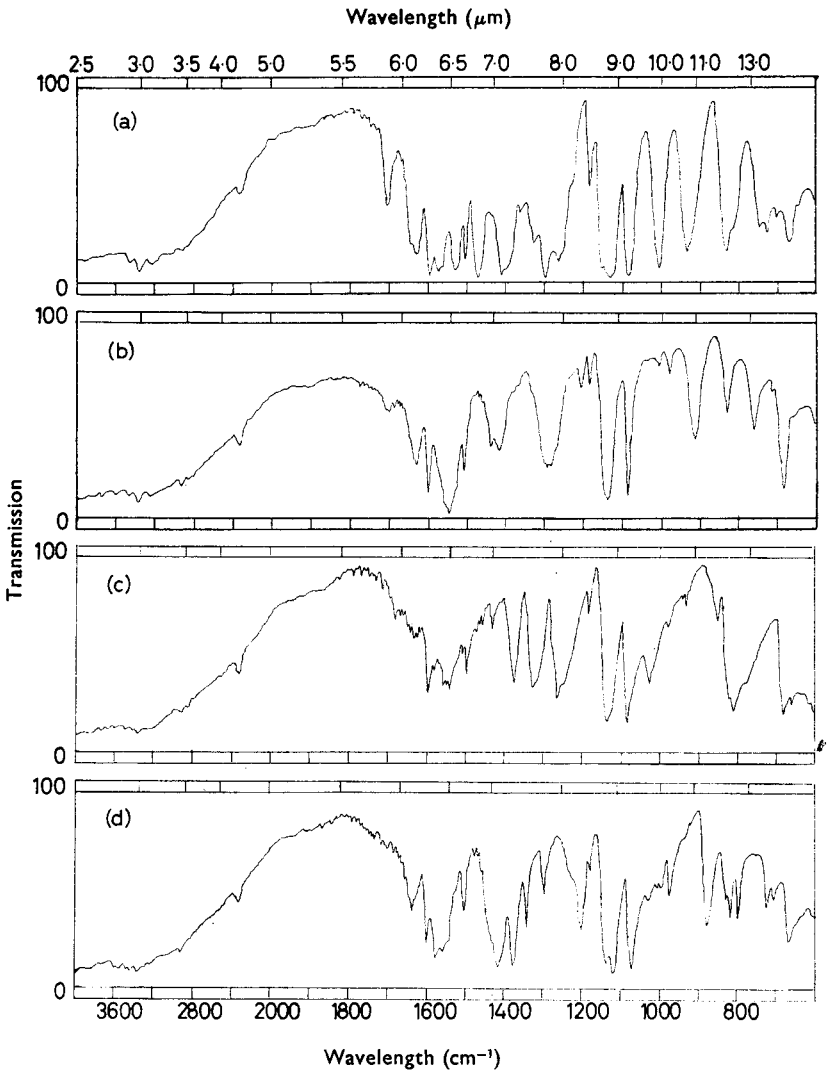

FIG. 2. ATR spectra of evaporated acetone solutions of (a) sulphamethoxypyridazine and (b) sulphamethizole. ATR spectra of evaporated acetone suspensions of (c) sulphacetamide sodium and (d) sulphadimidine sodium.

ments and eye-drops were used in addition to aqueous solutions of varying strengths, from 5 to 30%.

Methods

The ATR spectra of sulphonamides were obtained after allowing 2–3 drops of an acetone solution (about 3 mg/ml) to evaporate on one side of the KRS-5 plate. To obtain a satisfactory spectrum the sample covered the short dimension of the plate and normally about one third of the long dimension. Sodium salts were either used as an acetone suspension or were dissolved in the minimum of water and the aqueous solution diluted with about eight volumes of acetone.

The ATR spectra of water and aqueous solutions were obtained by placing 1 drop on the KRS-5 plate and covering with a rectangular glass cover slip of suitable size.

Ointments and Nujol mulls were smeared on one side of the plate, about one third of the area of one side being covered for mulls and from one third to the complete area of one side for ointments.

RESULTS AND DISCUSSION

Although Potts (1963) states that ATR spectra may not be completely identical with transmission spectra and for solids they can be so distorted as to be nearly useless unless contact between sample and plate is extremely intimate, in the present experiments no great variations between transmission and ATR spectra were obtained with any of the sulphonamides investigated (see Fig. 1). In general it was found that in all spectra the positions and shapes of the main peaks in the region 4000–650 cm^{-1} were identical whether they were obtained by transmission or ATR. However, peaks due to NH stretching vibrations in the range 3500 to 3200 cm^{-1} were all less intense in ATR spectra especially in Nujol mulls where frequently the weaker peaks disappeared completely.

In Fig. 2a and b are shown examples of ATR spectra obtained with evaporation of acetone solutions of the sulphonamides on the reflector plate. Fig. 2 c, d show the spectra obtained using acetone suspensions of sulphacetamide sodium and sulphadimidine sodium respectively. Solution of these sodium salts in the minimum of water followed by dilution with acetone gave spectra identical to those shown in Fig. 2 c and d, apart from additional absorptions in the 3300 and 1640 cm^{-1} regions due to traces of water.

Although no attempt was made to obtain different polymorphic forms of any of the sulphonamides for comparison of their ATR spectra after treatment with acetone as above, two different commercial samples of sulphadiazine, sulphadimidine, sulphadimidine sodium and sulphacetamide sodium gave spectra identical to those obtained from the respective Authentic Specimens.

In Fig. 3 the ATR spectrum of distilled water shows that there is sufficient transmittance in the region 1550–900 cm^{-1} to enable identification of the spectra of sulphacetamide sodium and sulphadimidine sodium in aqueous solutions. Katlafsky & Keller (1963) used a 40° Intran-2 prism for analysis of aqueous solutions and found that concentrations of at least 20% were required to obtain suitably intense spectra. They also found that this particular prism greatly decreased the intensity of the HOH deformation at 1640 cm^{-1}, allowing detection of aromatic absorption in the 1600 cm^{-1} region. With concentrations of 10% sulphacetamide sodium and

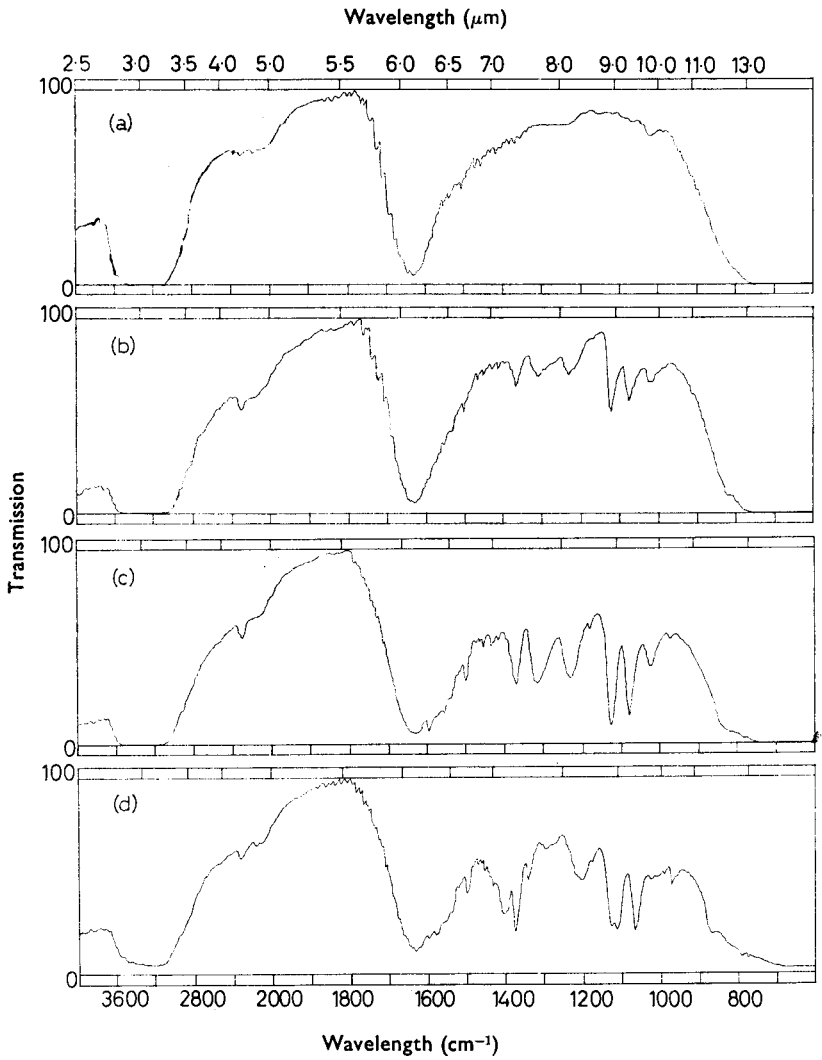

FIG. 3. ATR spectra: (a) distilled water, (b) aqueous solution of sulphacetamide sodium (5%), (c) aqueous solution of sulphacetamide sodium (20%), (d) aqueous solution of sulphadimidine sodium (10%).

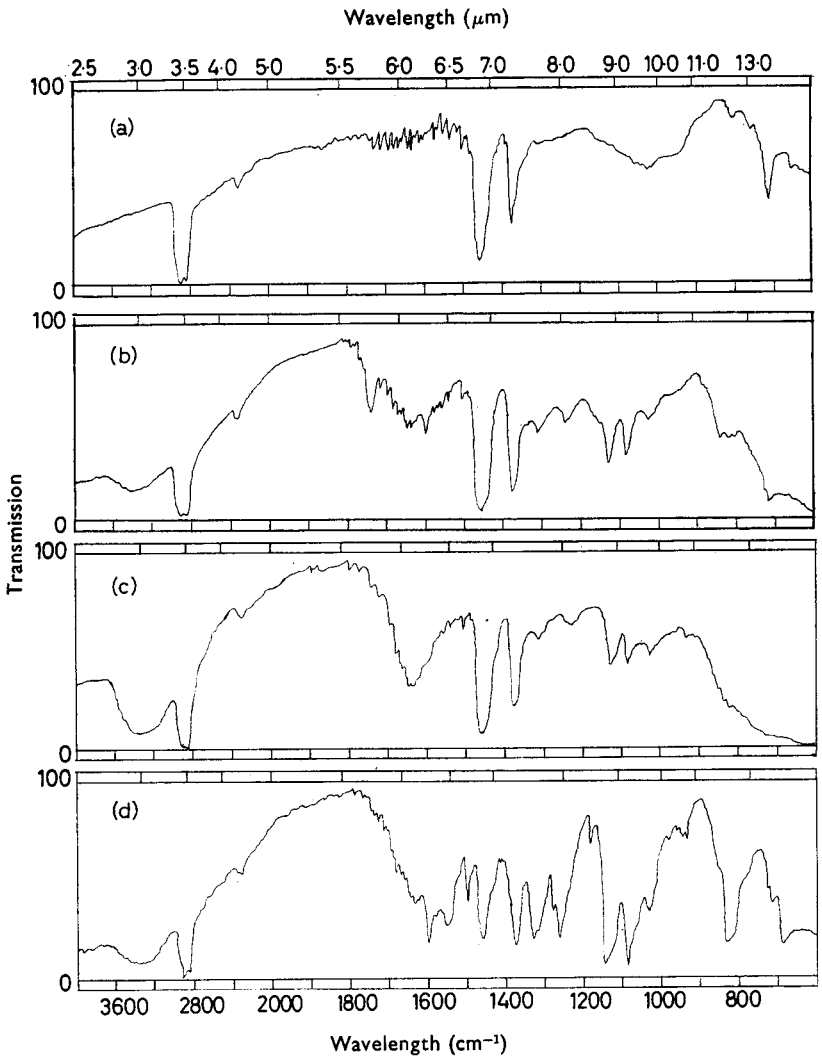

FIG. 4. ATR spectra: (a) ointment base, B.P., (b) sulphacetamide eye ointment, B.P., and proprietary ointment (c, 2½%: d, 10%).

using a 45° KRS-5 plate this absorption usually appears as a shoulder in the strong 1640 cm^{-1} absorption band, but even with concentrations of 15% there is a distinct peak. With 5% solutions the six main bands in the 1400–1000 cm^{-1} region are still distinct and characteristic enough for identification (see Fig. 3).

Identification of sulphacetamide sodium in eye-ointments was found to be easy in concentrations of 6% (B.P. sample) and 10%, but much less so in 2½% concentration where only the three peaks in the 1150–1000 cm^{-1} range are obvious (Fig. 4). However the complete absence of these latter peaks (and others) in a proprietary sample of sulphacetamide eye ointment B.P. examined was taken as proof that little or no sulphacetamide sodium was present.

The present investigation has shown that use can be made of attenuated total reflection to rapidly identify the sulphonamides investigated, either by using an Authentic Specimen for comparison or by direct comparison with standard transmission spectra. The ease of obtaining spectra of sulphacetamide sodium in ointments or aqueous solutions could be extended for ointments to give some quantitative estimate of the amount of drug present.

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