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Infrared spectroscopy using attenuated total reflection

I. P. S. KANG, C. E. KENDALL AND R. W. LEE

National Biological Standards Laboratory, P.O. Box 462, Canberra City, A.C.T. 2601, Australia

An ATR method is given for the examination of pharmaceuticals in the solid state as a layer of crystals on adhesive tape. Representative spectra are chosen to compare with, and to indicate advantages over, disc and mull techniques. Application of the method to pharmaceutical formulations is illustrated by the direct spectral identification of amodiaquine hydrochloride in tablet formulation.

Since the original development of attenuated total reflection (ATR) (Fahrenfort, 1961), the technique has been widely applied where transmission spectra are difficult to obtain (Katlafsky & Keller, 1963; Pawlak, Fricke & Szymanski, 1967; Wilks & Hirschfield, 1967). Apart from its straightforward use in the identification of sulphonamides and barbiturates (Edwards, 1971; Atkinson, 1971), little use has been made of the ATR technique in the examination of powders or crystalline materials as such. Adhesive tape for sample mounting has previously received brief mention (Harrick, 1967); no details of the technique have appeared however.

Apparatus

Infrared spectra were recorded either on a Perkin-Elmer 237, 257 or 457 grating infrared spectrophotometer. For the multiple ATR spectra a Perkin-Elmer multiple internal reflection attachment (F.M.I.R./050173) was used, with a 45° KRS-5 (thallous bromide-iodide) reflection plate (50 × 18 × 2 mm) which provided 25 reflections. For the single reflection ATR spectra the same multiple internal reflection attachment was used with a 45° KRS-5 prism. The energy difference between sample and reference beams was balanced by means of a beam attenuator in the reference beam.

Materials

All substances were either B.P. Authentic Specimens, B.C.R.S., International Reference Substances or manufacturer's standards.

The sample is pressed firmly on the tape (Scotch Tape No. 600 is preferred) by scraping with a scalpel held almost horizontal, and making a number of strokes until a uniform deposit is obtained. Reasonable but not excessive pressure is needed—there is a characteristic detachment and rolling up of the adhesive if too much pressure is applied. When the layer is uniform a few strokes with the scalpel blade almost vertical are made to remove the surplus sample. The tape is placed on the reflecting surface (sample side in contact) and fitted between rubber gaskets in the sample holder. Reasonable pressure is applied by tightening the clamping screws, leaving for a few minutes and then releasing. The tape adheres to the plate sufficiently to allow fitting in the open type mount. A properly prepared tape is translucent, becoming almost transparent when placed on the reflecting element.†

† A tape of width equal to the available reflecting surface is used.

Spectra from complete layers of crystals rarely show any interference from the natural rubber adhesive on the tape.*

RESULTS AND DISCUSSION

The samples of spectra chosen illustrate various advantages or qualities of the technique. Thus ATR spectra show somewhat sharper bands than KBr disc spectra (spectra 1 and 2).

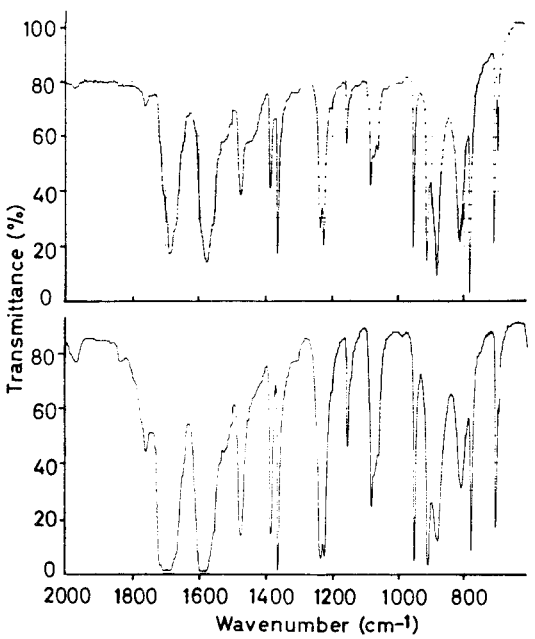
The distinction, for example, between the salt of an antibiotic and its free-acid form is not easy with liquid paraffin mulls or potassium halide discs. Identification of phenoxymethylpenicillin and its calcium salt (B.P. 1968) not only requires comparison of the sample spectrum with that of the Authentic Specimen but also tests to determine the presence or otherwise of calcium. By means of the ATR technique, however, the spectral differences between the free-acid form of phenoxymethylpenicillin (spectrum 3) and its potassium and calcium salts are so marked (spectra 4 and 5) that distinction between them requires no additional examination.

Definitive spectra have also been obtained for many antibiotics such as nystatin, polymyxin, erythromycin, kitasamycin, kanamycin, streptomycin, which are normally regarded as giving spectra of very poor quality.

Since the method described avoids grinding (necessary for halide discs or Nujol mulls), it may be safely used in the examination of substances where polymorphism occurs. A number of common drugs exhibits this phenomenon (*cf.* chloramphenicol palmitate, Anderson, 1966) and the spectra of polymorphs may differ appreciably. The ATR technique detailed above allows the spectrum of each stable polymorphic form to be recorded.

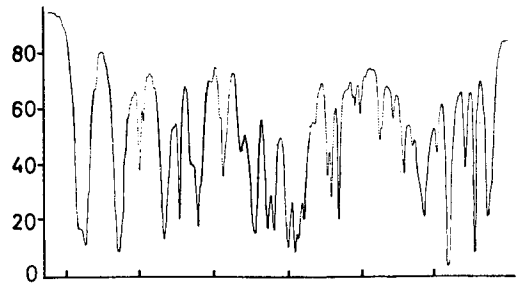
1. Allopurinol (ATR)

2. Allopurinol (KBr Disc)

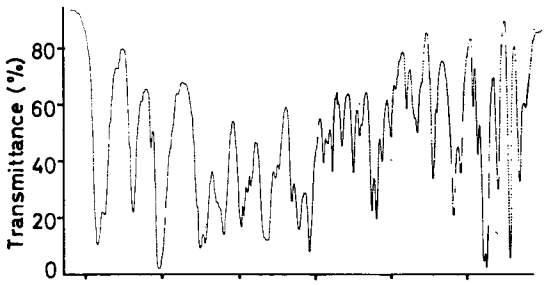


* Natural rubber is distinguished by bands at 2935, 2900, 2830, 1440, 1375, and 830 cm^{-1}.

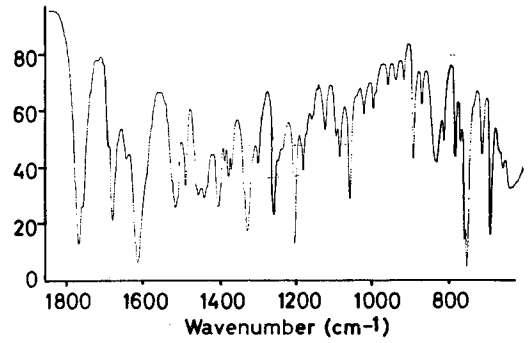
3. Phenoxymethylpenicillin



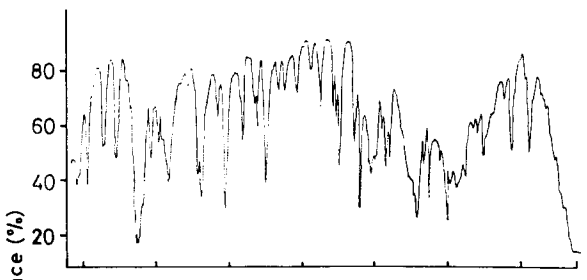
4. Phenoxymethylpenicillin potassium



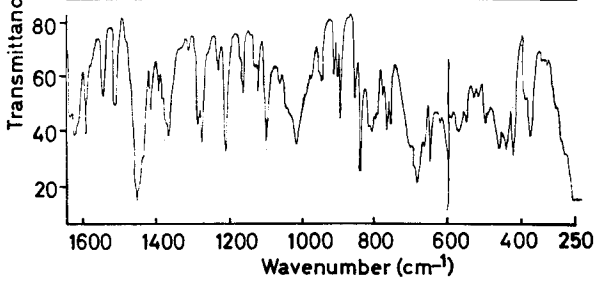
5. Phenoxymethylpenicillin calcium



6. Amodiaquine hydrochloride



7. Amodiaquine hydrochloride tablet (100 mg in 263 mg)



Where products contain about 25% or more of the active ingredient, identification can be made directly on preparations such as tablets or capsules, without extraction of the active component (spectra 6 and 7). Common excipients give rather featureless spectra (e.g. starch) while others (e.g. lactose) have a group of easily recognized bands (in the 1000 to 1200 cm^{-1} region in lactose) and their presence is readily allowed for. The ATR identification for phenethicillin potassium tablets and capsules is possible by this technique, and exceptionally valuable in that identification requires 30 min in contrast to the official B.P. 1968 method which requires approximately 5 h.

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