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The identification of tablets and capsules containing barbiturates by MATR infrared spectroscopy

J. E. ATKINSON

The School of Pharmacy, Robert Gordon's Institute of Technology, Aberdeen AB9 1FR, U.K.

The technique of MATR infrared spectroscopy has been used to record the infrared spectra of a variety of barbiturate-containing tablets and capsules. The production of different spectra for preparations containing different active ingredients, and the absence of spectral variations arising from the source of manufacture and the presence of tablet and capsule additives, indicate the technique to have possible application in the identification of tablets and capsules, especially where only small samples (1–2 mg) are available.

The introduction of the technique of attenuated total reflectance (ATR) to infrared spectroscopy and its modification to multiple attenuated total reflectance (MATR) have mainly found application in the examination of solid surfaces, like paper coatings and paints (Szymanski, 1967).

The technique involves the placing of the sample, which may be in the solid phase, against the surface of a plate that has suitable optical properties. For MATR the infrared light passes into the plate and, owing to the angle of incidence, dimensions of the plate, and refractive index of the material, undergoes a number of internal reflections. At each of these the light is able to penetrate the sample and undergo absorption thus making it possible to obtain an infrared spectrum for the sample.

In view of the sampling procedure, the technique was thought to have useful application in the identification of tablets and capsules. Preparations containing the barbiturate group of drugs were chosen because: (a) The barbiturates are closely related chemically. An examination of the spectra of tablets and capsules containing barbiturates would test the possibility of distinguishing between such preparations even though their formulation requires the addition of other substances (Remington, 1965). (b) Differences in the crystalline form of the barbiturates produced by grinding are known to produce variations in the halide disc infrared spectra of these compounds (Clarke, 1969). By using barbiturates the possible production of such differences during the process of tablet manufacture could be examined. (c) This technique had a possible use in tablet and capsule identification.

RESULTS AND DISCUSSION

The inclusion in tablets and capsules of diluents, disintegrants, binders and lubricants gives rise to the possibility that these compounds might contribute to the spectra of tablets and capsules. To examine this a batch of tablet granules was prepared containing (g) phenobarbitone sodium 60, lactose 296, starch 40, magnesium stearate 4 and 2% gelatin solution 50 ml. A corresponding batch of blank granules was also prepared. From these two batches of granules a number of phenobarbitone sodium

tablets (155 mg*; 23 mg†) and blank tablets (130 mg*; 0 mg†) were compounded. The MATR infrared spectrum of a sample of one of the phenobarbitone sodium tablets (1·5 mg‡) had major peaks at 1660, 1555, 1422, 1342, 1292, 1260 cm^{-1}. This spectrum was found to be identical with the MATR infrared spectrum of the batch of phenobarbitone sodium used to prepare the tablet granules. The spectrum of the blank tablet (5·6 mg‡) had no major peaks although a base line drift did occur in the ranges 4000–2000 and 950–650 cm^{-1}.

The possibility that proprietary phenobarbitone sodium tablets could differ from the formulation above and that this could alter the MATR infrared spectrum of the tablet was examined by running the spectrum of phenobarbitone sodium tablets (55–104 mg*; 30 mg†) produced by seven different manufacturers. The tablet spectra obtained were found to be identical with the spectrum obtained for the phenobarbitone sodium tablets prepared as described above. To examine further any possible differences in the MATR infrared spectrum of tablets due to variations in manufacture, the spectra of phenobarbitone tablets (57–87 mg*; 30 mg†) from eight manufacturers were run and found to be identical. The spectrum of phenobarbitone tablets had major peaks at 1702, 1419, 1350, 1312 and 1224 cm^{-1}. A comparison of the MATR infrared spectrum of the phenobarbitone sodium tablets and the phenobarbitone tablets indicated that this method of analysis could be used to distinguish between them.

Table 1. *The main peaks in the MATR infrared spectra of tablets and capsules containing one pharmacologically active compound and the weight of sample required to obtain an MATR infrared spectrum in relation to the weight of the tablet and the weight of the active ingredient.*

Barbiturate tablet	Wavelength (cm^{-1})	Wt of tablet or capsule content (mg)	Wt of active ingredient (mg)	Wt of sample (mg)
Amylobarbitone	1695, 1425, 1375, 1352, 1310, 1265, 1237, 1207, 1162, 1042, 815	80	30	0·6
Amylobarbitone sodium (Amytal sodium)	1699, 1609, 1559, 1425, 1369, 1335, 1315, 1285, 1260, 1155, 1050, 995, 788, 758	715	200	0·9
Barbitone	1757, 1667, 1408, 1372, 1315, 1229, 1039, 937, 860	425	324	1·5
Barbitone sodium (Medinal)	1695, 1662, 1540, 1456, 1445, 1430, 1410, 1370, 1335, 1310, 1015, 840, 787, 747	399	320	3·0
Butobarbitone	1697, 1422, 1357, 1304, 1237, 1209, 1032, 794	142	100	0·4
Cyclobarbitone	1689, 1409, 1339, 1289, 1209, 1026,	332	194	0·3
Hexabarbitone	1715, 1441, 1375, 1355, 1270, 1200, 1044, 775	342	260	0·5
Pentobarbitone sodium (Nembutal)	1693, 1658, 1650, 1553, 1425, 1350, 1308, 1257	128	30	0·6
Phenobarbitone	1702, 1419, 1350, 1312, 1224, 1336, 764, 692	93	30	0·7
Phenobarbitone sodium	1695, 1660, 1555, 1422, 1342, 1292, 1260, 1032, 777, 686	69	32	0·6
Quinalbarbitone sodium (Seconal sodium)	1693, 1655, 1551, 1426, 1336, 991, 921, 786	109	50	0·9
Nealbarbitone (Censedal)	1695, 1435, 1365, 1320, 1270, 1215, 1030, 992, 932, 842	84	60	0·4

* Total weight of tablet.
† Weight of the active ingredient in the tablet.
‡ Weight of sample used to obtain spectrum.

All of the tablets that had so far been examined were plain white and if the technique is to have wide application in tablet and capsule identification the addition of colouring agents and coatings to these preparations should ideally not affect the MATR infrared spectrum. To examine coloured tablets the spectrum of a pink butobarbitone tablet (142 mg*; 100 mg†), a dark pink Soneryl tablet (249 mg*, 100 mg†) and butobarbitone were examined and found to be identical. The spectrum of a Spansule (286 mg*; 97 mg†), a capsule containing phenobarbitone as white and blue granules, was identical with the spectrum previously obtained for phenobarbitone tablets. Secondly the spectrum of a Berbenzyl-30 tablet (93 mg*; 30 mg†), a dark red coated tablet, was identical with one previously recorded for phenobarbitone tablets. The possible effect of tablet coatings was further investigated using a blue-coated amylobarbitone sodium tablet (718 mg*; 200 mg†). The spectrum was run for a crushed tablet and a sample of the inner white core. Both spectra along with that obtained for the white powder present in an amylobarbitone capsule (219 mg*; 200 mg†) were identical.

Table 2. *The main peaks in the MATR infrared spectra of tablets and capsules containing more than one pharmacologically active compound and the weight of sample required to obtain an MATR infrared spectrum in relation to the weight of the tablet and the weight of the active ingredient.*

Tablet	Wavelength (cm^{-1})	Wt of tablet or capsule content (mg)	Wt of active ingredient (mg)	Wt of sample (mg)
Carbrital	1692, 1547, 1427, 1369, 1092	437		0·6
Pentobarbitone			100	
Carbromal			250	
Epanutin and phenobarbitone	1708, 1552, 1392, 1347, 1292, 1012	152		0·3
Epanutin			100	
Phenobarbitone			50	
Nembudeine	1694, 1650, 1600, 1550, 1538, 1505, 1470, 1451, 1410, 1365, 1240, 1112, 920, 822, 790	619		1·3
Codeine sulphate			15	
Aspirin			210	
Phenacetin			150	
Caffeine			30	
Nembutal			15	
Phenobarbitone and theobromine	1691, 1537, 1411, 1346, 1299, 1218, 1026	437		1·3
Phenobarbitone			30	
Theobromine			300	
Sonalgin	1701, 1658, 1602, 1551, 1506, 1480, 1445, 1411, 1370, 1321, 1241, 1173, 1114, 1045, 922, 835, 733	604		1·7
Butobarbitone			60	
Phenacetin			225	
Codeine Phosphate			10	
Sonergan	1693, 1408, 1351, 1300, 1233, 1030	303		0·8
Promethazine HCl			15	
Butobarbitone			75	
Tuinal	1691, 1651, 1544, 1429, 1309, 1151, 987, 915, 730	165		0·8
Quinalbarbitone sodium			50	
Amylobarbitone sodium			50	

In view of these findings, the MATR infrared spectra of a number of capsules and tablets containing a barbiturate as the only pharmacologically active ingredient were

run. The main peaks in the spectra of these tablets and those for the previously examined barbiturate tablets are recorded in Table 1. The spectra of a variety of capsules and tablets containing a barbiturate with other pharmacologically active ingredients have been examined and the main peaks in these spectra are presented in Table 2. An examination of the results in Tables 1 and 2 shows that it is possible to obtain infrared spectra of tablets and capsules using the MATR technique for sample presentation. These spectra are characteristic of a particular pharmacologically active ingredient or combination of ingredients and are not affected by the presence of tablet and capsule additives. The demonstration of a correlation between the spectra of a barbiturate and a tablet containing that drug, as with phenobarbitone sodium and

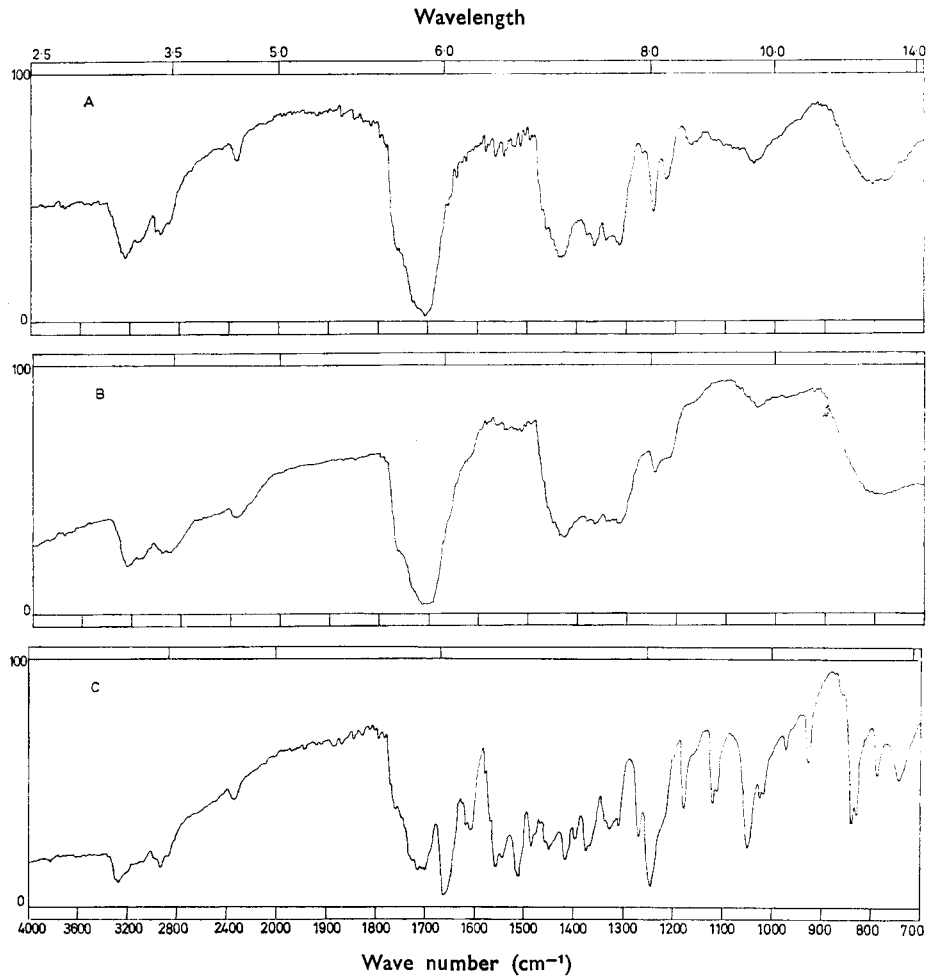

FIG. 1. The MATR infrared spectra of (a) Butobarbitone tablet, (b) Butobarbitone B.P. and (c) Sonalgin tablet.

butobarbitone could have useful application in tablet identification (see Fig. 1). This application would be limited to some extent by the number of types of tablet on the market containing only one pharmacologically active ingredient. The wider application of the technique to the identification of an unknown tablet would

necessitate the running of many reference tablet and capsule spectra. The recording of this spectral information using the method suggested by Curry, Read & Brown (1969), supplemented with other information, such as the shape, colour and size of the capsule or tablet, could be used as a rapid method of capsule and tablet identification.

METHODS

Instrument. Spectra were run on a Hilger and Watts Infrascan Spectrophotometer, fitted with a MIR-1 Teflon (Wiltec Scientific) internal reflector holder and a KRS-5, 2 mm, 45° reflector plate. An AT-30 (RIIC) attenuator was fitted in the reference beam. The energy level of the instrument was set at X2 and a scan time of 16 min was used. A wavelength correction was applied to each spectrum using a polystyrene film as a reference standard.

Sampling technique. The tablet or capsule content was crushed and a sample (Tables 1 and 2) was placed on one side of the KRS-5 plate. One to two drops of acetone were added to the sample and allowed to evaporate at room temperature (21°).

The placing of a sample of the crushed material against both sides of the KRS-5 plate which was then held in a MIR-2 (Wiltec Scientific) solid sample holder was found to give very poor spectra.

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