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Comparison of the nuclear magnetic resonance and infrared spectroscopic methods for the quantitative analysis of polydimethylsiloxane

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A method based on nuclear magnetic resonance spectroscopy is described for the quantitative determination of polydimethylsiloxane (PMS) in a variety of pharmaceutical preparations. An extraction procedure using deuterochloroform within the sample tube was devised. In the presence of an internal standard, the PMS concentration was determined directly using integrated peak areas, without the necessity of establishing calibration curves. Accurate quantitative results were achieved with samples containing at least 2mg PMS, extracted from formulations containing greater than 0·5% PMS. The extraction procedure and nmr assay were both more efficient and convenient than the B.P.C. method.

Polydimethylsiloxane (PMS) may be quantitatively determined by a number of methods viz. atomic absorption (Mario & Gerner, 1968; Miller, Helprin & Finlayson, 1969) and infrared spectroscopy (Pozefsky & Grenoble, 1957; Horner, Weiler & Angelotti, 1960; Gantes, Barat & Joly, 1970; Rihs, 1971). Extraction into toluene and measurement of the infrared absorption intensities at 1250 cm^{-1} now forms the basis of the British Pharmaceutical Codex (1973) method for creams. None of these methods are specific for PMS, and all are subject to interference from other components of formulations.

Nuclear magnetic resonance spectroscopy (nmr) has already been used for the quantitative analysis of a wide range of pharmaceuticals (Kram & Turczan, 1971) and other substances (Kasler, 1973). It has the advantages that the spectral information is structurally specific and integrated peak areas are directly proportional to the quantity of substance present. We have therefore investigated its application to the assay of PMS in pharmaceutical formulations.

MATERIALS AND METHODS

A variety of pharmaceutical preparations were selected to cover a wide range of PMS concentrations and viscosities. These preparations were obtained either commercially or from stocks supplied to this laboratory.

Cream

A cream (I) was stated to contain 20% PMS-350 and also 0·05% hydrargaphen equivalent to 0·02% organically combined mercury.

Another cream (II) was stated to contain 3·0% PMS-100, 1% Fentichlor and 1% urea in a lanolin base.

Other formulations

The fluid from an aerosol spray (III) was stated to be PMS-1000 containing 0·5% aluminium dihydroxyallantoinate and 0·02% cetyl pyridinium chloride. A suspension (IV) was stated to contain 0·5% PMS, 4% w/w aluminium hydroxide, 4% w/w magnesium hydroxide in a spearmint flavoured medium. Tablets (V) were stated to contain 10% PMS-1000 together with 44% w/w sucrose, 20% w/w sorbitol, 20% w/w aluminium hydroxide and 0·6% w/w silica.

Infrared spectroscopic assay

The PMS content was assayed according to the British Pharmaceutical Codex 1973. The suspension and the creams were mixed with anhydrous sodium sulphate to remove water and the PMS extracted by repeated washings with cold toluene. The aerosol fluid and tablets did not require drying before extraction. With those samples containing small concentrations of PMS, it was necessary to concentrate the extracts by partial evaporation in a rotary evaporator. One portion of the suspension (IV) was extracted with chloroform instead of toluene; the chloroform was evaporated and replaced with toluene for spectroscopy. Infrared spectra were recorded on a Perkin Elmer 621 double beam spectrophotometer, using liquid cells with sodium chloride windows (path length 3 mm). Compensation for absorption by the solvent (and extracted liquid paraffin, where present) was achieved by suitably adjusting a variable path cell containing those materials in the reference beam. The intensity of the absorption at 1260 cm^{-1} ($Si\text{-}CH_3$) was used with a calibration graph to determine the PMS present in the extracts. The linear calibration plot of optical density against PMS concentration was obtained using 0·2, 0·4, 0·6, 0·8 and 1·0% w/w solution of PMS in toluene. The toluene and chloroform were of Analar grade (Fisons).

Nmr spectroscopic assay

A survey spectrum was taken of any formulation that had not previously been so examined. A portion of the sample was placed in a nmr tube together with 0·5 ml $CDCl_3$; after capping the tube, it was shaken periodically for 10 min and then the $CDCl_3$ layer allowed to settle into the bottom of the tube. The 60 MHz proton spectrum of this layer was then recorded with a JEOL C-60HL spectrometer with an ambient probe temperature of 32°.

When the resonance positions of the components of the sample had been ascertained, an internal standard was selected so as to be observable in an otherwise unoccupied portion of the spectrum. Either hexamethylbenzene (VI, $\delta = 2{\cdot}15$ ppm, proton equivalent weight = 9·01), or *p*-dichlorobenzene (VII, $\delta = 7{\cdot}23$ ppm, proton equivalent weight = 36·75), were suitable in that the absorption signals were readily integrated in all samples examined.

Portions of the sample and standard were each accurately weighed into a sample tube, so that for each milligram of PMS stated to be in the sample portion, approximately 0·67 mg VI or 3·0 mg VII was present. Sufficient sample was used for there to be 2–20 mg PMS in the sample tube. The same $CDCl_3$ extraction procedure was used as above and the nmr spectrum was recorded.

This procedure gave a spectrum in which the absorption peaks of the PMS and internal standard were of approximately equal area, both for accuracy and convenience. These peak areas were integrated five times each at a sweep rate of 11 Hz s^{-1}.

The average PMS integral, I(pms), and that of the internal standard I(s) were applied in the formula:

$$\% \text{ weight PMS} = \frac{\text{wt standard}}{\text{wt sample}} \times \frac{\text{p.e.w. PMS} \times \text{I (pms)} \times 100}{\text{p.e.w. standard} \times \text{I (s)}}$$

The proton equivalent weight (p.e.w.) of a substance is the molecular weight of the molecule or polymer unit divided by the number of protons responsible for the resonance absorption of interest (i.e. PMS has a p.e.w. = 12·33).

$CDCl_3$ was obtained from British Oxygen Company and had isotope purity of 99·8%; CCl_4 was Analar grade from Fisons. Hexamethylbenzene (99·90%) and *p*-dichlorobenzene (99·92%) were obtained from the High Purity Organic Standard range of the National Physical Laboratory. PMS-350 was obtained from Hopkin and Williams Ltd.

RESULTS

Determination of weighed quantities of PMS, (Table 1) show that the nmr procedure provides accurate results. Following extraction in the nmr tube, the application of this procedure to the determination of PMS in a variety of formulations, (Table 2) shows a precision with standard deviation of the mean at a 95% confidence limit for formulations I, IV and V of 0·2, 0·05 and 0·2% PMS respectively. Generally the PMS content was greater than that found by the B.P.C. infrared method and in good

Table 1. *Determination of PMS by nmr spectroscopy.*

PMS weighed (mg)	PMS found (mg)	Recovery (%)
3·31	3·33	100·6
6·40	6·48	101·2
9·78	9·70	99·2
12·58	12·38	98·4
12·65	12·71	100·5
15·97	15·87	99·4
18·41	18·35	99·7
18·40	18·49	100·7

Average 99·9 Standard deviation = 0·9

Table 2. *Assay of formulations containing PMS by nmr and infrared spectroscopy.*

Sample	Nominal PMS content[1] % w/w	PMS recovered Nmr % w/w	B.P.C. Infrared % w/w
I Cream	20·0	19·7, 19·7, 19·7 19·4, 19·8 (s.d. = 0·2)	19·0, 18·6
II Cream	3·0	2·86, 3·01	1·48, 2·39
III Liquid	99·5	100·6, 100·9	98·0, 98·5
IV Suspension	0·50	0·457, 0·460, 0·542 0·529, 0·498 (s.d. = 0·05)	0·21, 0·19 0·28[2]
V Tablet	10·1	9·98, 9·86, 10·10 9·87, 9·78 (s.d. = 0·2)	7·8, 6·8

[1] Declared by manufacturer.
[2] PMS extracted with $CHCl_3$.

agreement with the declared content. In the case of the tablets (V) a mean content of 9·92% w/w was found; the presence of 0·6% w/w of silica had little effect on this result although Buist, Burton & Elvidge (1973) have shown that silica can retain a quantity of PMS equivalent to at least 0·1% by weight of the tablet in this formulation. Quantitative extraction of PMS was confirmed (Table 3) by the assay of samples of cream I to which weighed amounts of PMS (2–15% w/w) had been added.

Table 3. *PMS extraction from creams in nmr tube.*

Sample	PMS in cream[1] (% w/w)	PMS recovered[2] (% w/w)
Ia	21·8	21·6
Ib	23·4	23·5
Ic	24·4	24·1
Id	27·0	26·6
Ie	31·2	30·9
If	35·0	35·0

[1] Calculated on basis of cream I containing 19·7% w/w PMS.
[2] Single determinations.

DISCUSSION

The nmr spectroscopic assay of PMS is not hindered by interfering materials unlike that of the infrared-based B.P.C. method, and also does not require calibration curves. A particular advantage is that extraction *within the sample tube* was found to be feasible with deuterochloroform as solvent. The density of deuterochloroform ensures that, in the tube, a lower layer containing PMS forms in the only part being monitored by the spectrometer; separation of layers is thereby unnecessary. In this manner, deuterochloroform achieved a rapid and complete extraction (< 10 min) unobtainable in the B.P.C. method.

The nmr assay can be extended to formulations containing less than 0·5% PMS either by co-adding spectra in a computer or by performing a pre-extraction of a larger volume of formulated material outside the nmr tube. Use of other standards can be expected to allow assays of formulations which contain components interfering with standards VI or VII.

Thus, nmr spectroscopy provides a basis for an accurate and specific assay of PMS. Deuterochloroform extraction of PMS within the nmr tube is more efficient than the existing B.P.C. method and can be used for a wide variety of formulations.

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