RED STAINING OF SKIN DUE TO CONTAMINATED METHY ETHYL KETONE

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SYNOPSIS

A total of 106 workers from 4 factories developed a red staining of the hands (particularly the fingers) after repeated contact with certain batches of commercial methyl ethyl ketone (MEK). The non-volatile contaminants obtained by distillation of the MEK produced a similar red discoloration during in vitro skin tests. Dibutyl phthalate and dioctyl phthalate were identified by gas chromatography/mass spectrometry to be two of the components of the non-volatile contaminants. Dibutyl phthalate in the presence of MEK distillate produced a pink staining during in vitro skin tests.

INTRODUCTION

A total of 106 workers (93 females and 13 males) from 4 factories developed a red staining of the hands (particularly the fingers) after repeated contact with certain batches of commercial methyl ethyl ketone (MEK). An investigation was conducted to determine the cause of this phenomenon.

CASE REPORTS

The first factory 'A' was engaged in servicing of aeroengines and was using MEK as a paint stripper. In Aug 80, 10 of the workers developed a red staining of the hands. They had been using nylon pads (Scotch Brite) soaked with MEK to remove paint from aircraft parts. Polyvinyl gloves were provided but were apparently not effective. In Apr 79, nine of the workers were similarly affected. No hand protection was provided at that time.

The second factory, an electronics company 'B', was affected in late Nov and early Dec 80. The workers involved (93 females) were using MEK, in a mixture with ethyl acetate (EA) and isopropyl alcohol (IPA), to remove unwanted uncured epoxy coating ink markings from small integrated circuits and printing equipment. In most cases, small brushes or cotton buds were used to apply the solvent mixture on the markings. In a few cases, the circuits were placed in small cages and dipped directly into the solvent mixture. Some of the workers used tissue soaked with the solvent mixture and even used the mixture to wash their hands. Most of the workers wore finger cots and/or cotton gloves but some contact with the solvent mixture was unavoidable as the circuits had to be handled.

The third establishment was a chemical factory 'C' which sold the solvent mixture containing MEK to factory 'B'. The affected worker was involved in preparing the mixture from drums containing the individual solvents (MEK, EA and IPA) and transferring the mixture to tins. No hand protection was used. He developed the red staining sometime in Nov 80.

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The fourth establishment was another chemical factory 'D' which sold MEK to factory 'A' and MEK, EA and IPA to factory 'C'.

The MEK was imported in 300 to 400 metric ton shipments approximately once every 3 months. The solvent was piped from ship tanks to the shore tanks of the main importing company 'E' and subsequently transferred via road tankers to storage tanks in factory 'D'. As and when required the MEK would be transferred via metal pipes into 200 litre metal drums for sale. The 2 affected workers in factory 'D' were involved in transferring MEK from the storage tanks into drums. No hand protection was used. They apparently noticed slight red staining of the hands off and on during 1980 and also in late 1979.

In all the 4 factories, the workers had handled other batches of MEK without experiencing red staining effects. The batches which were implicated were noticed to be slightly cloudy on visual inspection compared with previous batches which were clear.

CLINICAL FEATURES

The skin staining generally appeared about 4 to 5 days after the first contact with the MEK and began as a pinkish discoloration. This deepened to a rose-red colour with repeated contact (Figure 1 a) - c)). In most cases the staining persisted for 1 to 3 weeks, fading gradually after contact stopped and disappearing completely after about a week. Except for a few cases, no eczema accompanied the red staining. The exceptions were those who had used the MEK to wash their hands and developed an irritant contact dermatitis in addition to the staining.

None of the affected workers had any systemic symptoms. No MEK or IPA was detected in the workroom air of factory 'B'. The EA air concentration was 50 ppm, well below the Threshold Limit Value of 400 ppm (1). No environmental assessments were carried out in factories 'A', 'C' and 'D' because the solvents were handled in open well-ventilated areas and for relatively short periods.

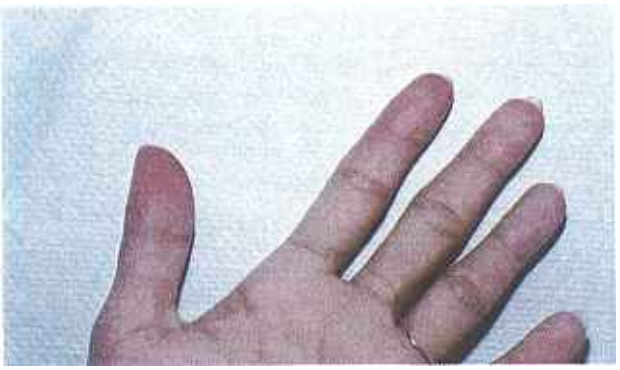


Figure 1 a) Red staining of fingers

METHODS AND RESULTS

Non-volatile Contaminants

As different batches of MEK from different shipments seemed to be implicated, samples (where available) from 4 different shipments (received between Aug 80 and Oct 81) were analysed for non-volatile contaminants. The samples were obtained from various locations, as follows:

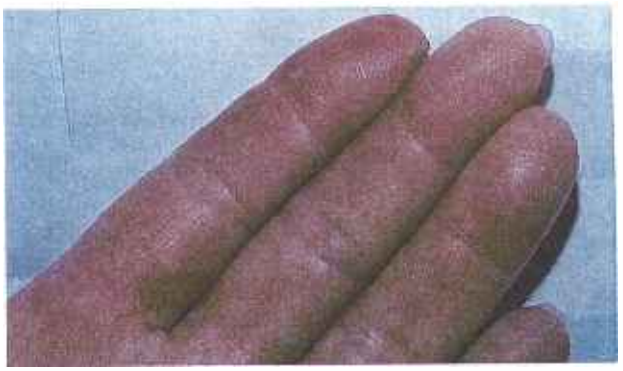


Figure (b) Red staining of fingers

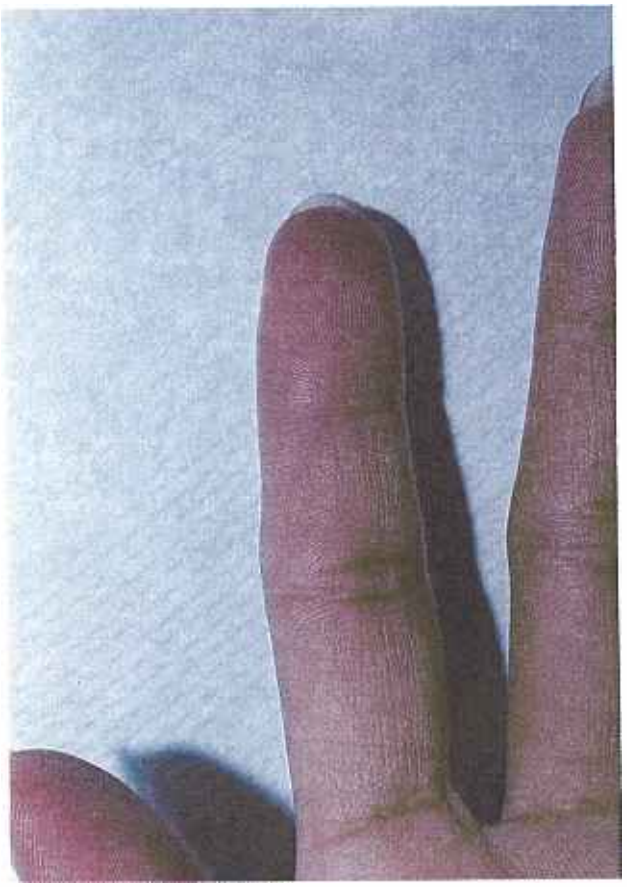


Figure (c) Red staining of fingers

	Source	Sample Description[a]		No. of Samples
1	Ship tank	(i)	Cloudy[b]	1
		(ii)	Clear	2[c]
2	Shore tank (Factory 'E')	(i)	Cloudy[b]	1
		(ii)	Clear	1
3	Storage tank (Factory 'D')	(i)	Clear	2[d]
4	Drum	(i)	Cloudy	4
	(Factories 'C' and 'D')	(ii)	Clear	2

a : "Clear" and "Cloudy" refers to Colour (APHA) $\leqslant 10$ and > 10 respectively (ASTM D740 specification) using ASTM D1209 test (2).

b : Samples were originally clear on receipt of shipment but apparently turned cloudy following 3 months of storage.

c : Includes one slop sample.

d : Includes one sample direct from storage tank and one obtained after passage through metal pipe (i.e. prior to drum).

Samples of analytical reagent grade MEK (MEK GR grade from MERCK) (3), and commercial grade IPA and EA (from factories 'C' and 'D') were also analysed for non-volatile contaminants.

100 ml each of all the above mentioned samples were distilled at temperatures slightly above the respective boiling points of the solvents, viz MEK: 79.6°C, IPA: 82.5°C and EA: 77°C (4). The resultant distillates (volatile components) and non-volatile residues were collected.

The distillates and the non-volatile residues of the various samples were analysed by gas chromatography/mass spectrometry (GC/MS) under the following experimental conditions:

Instrument	:	Hewlett-Packard Model 5985
GC Column	:	3% oV-1 glass column operated at 240°C
Carrier gas	:	helium
Mass spectrometer	:	electron impact mode

No significant volatile impurities could be detected in the distillates of the respective solvents.

In all the drum samples of MEK the non-volatile residues were found to contain dibutyl phthalate (DBP) and/or traces of dioctyl phthalate (DOP). Examples of the total ion chromatograms of the non-volatile residues from the "cloudy" and "clear" MEK (drum samples) and commercial grade DBP and DOP are shown with the mass spectrograms of the respective peaks in Figures 2 to 5 respectively. No contaminant could be identified in the MEK samples from the ship, shore or storage tanks (whether "cloudy" or "clear"), or in the MEK GR grade, IPA and EA samples.

The percentages of non-volatile matter in the MEK (drum) and MEK (GR grade) samples were determined according to British Pharmacopoeia 1973 (5), i.e. a known volume of MEK was evaporated in a water-bath and dried to constant weight at 105°C.

The non-volatile residue content of the above-mentioned MEK samples were as follows:

	Sample	Non-volatile matter (% w/v)
1	"Clear" MEK (drum) sample	0.018
2	"Cloudy" MEK (drum) samples	0.020 – 0.041
3	MEK (GR grade)	0.008

In vitro skin tests

To ascertain if the non-volatile contaminant(s) could have produced the red staining effect, in vitro skin tests were carried out. The following samples were used:

Sample Type	Sample Description
1	"Cloudy" MEK (drum and tank samples)
2	"Clear" MEK (drum and tank samples)
3	MEK (GR grade)
4	Distilled water
5	Distillate of "Cloudy" MEK (drum samples)
6	Distillate of "Clear" MEK (drum samples)
7	Non-volatile residues of "Cloudy" MEK (drum samples)
8	Non-volatile residues of "Clear" MEK (drum samples)
9	DBP in distilled water
10	DBP in distillate of "Clear" MEK
11	DBP in IPA
12	DBP in EA
13	DOP in distilled water
14	DOP in distillate of "Clear" MEK

All samples were placed in 3 ml screw capped glass vials, each containing a thin piece of human skin, mainly stratum corneum, from the sole (less than 1 cm diameter). All the vials were incubated at 37°C for 24 hours and then allowed to cool to room temperature. Any colour changes in the skin specimens were noted.

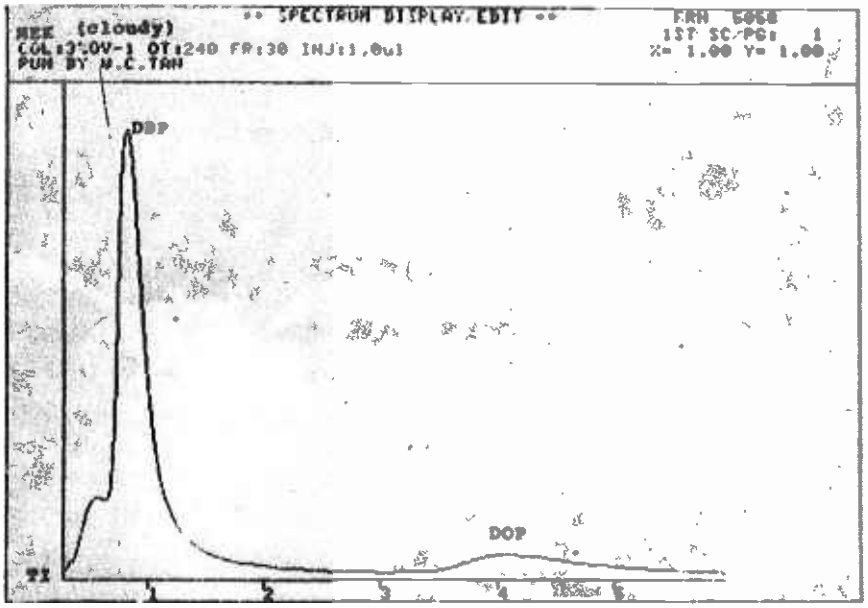
For samples 1 to 6, 1 ml of the liquids was used. For samples 7 and 8, the residues were placed in 1 ml distilled water. For samples 9 to 12, 0.1 ml DBP was placed in 1 ml of distilled water, distillate of MEK, IPA and EA respectively. For samples 13 and 14, 0.1 ml DOP was placed in 1 ml of distilled water and distillate of MEK respectively. The DBP and DOP were commercial grade samples from factory 'D'.

All the MEK drum samples ("cloudy" and "clear") and the resultant non-volatile residues identified earlier by GC/MS to contain DBP produced a red staining effect on the skin specimens. One MEK drum sample which was shown to contain DOP and only traces of DBP did not produce the red staining at 24 hours but caused a pink staining after 36 hours. Another MEK drum sample which was shown to contain DOP but no DBP did not cause any staining.

None of the ship, shore or storage tank MEK samples, distillates of MEK drum samples, MEK (GR grade), distilled water or DOP samples produced any staining effects. Of the DBP samples, only that used in the distillate of MEK caused a pink staining effect. Those used with distilled water, IPA and EA did not produce any staining effect. (Figure 6).

DISCUSSION

As far as we are aware, MEK has not been reported to cause red staining effects on the skin, although its irritant effects have been documented (6). DBP and DOP have also not been reported to cause such staining effects. As a group, the phthalate esters



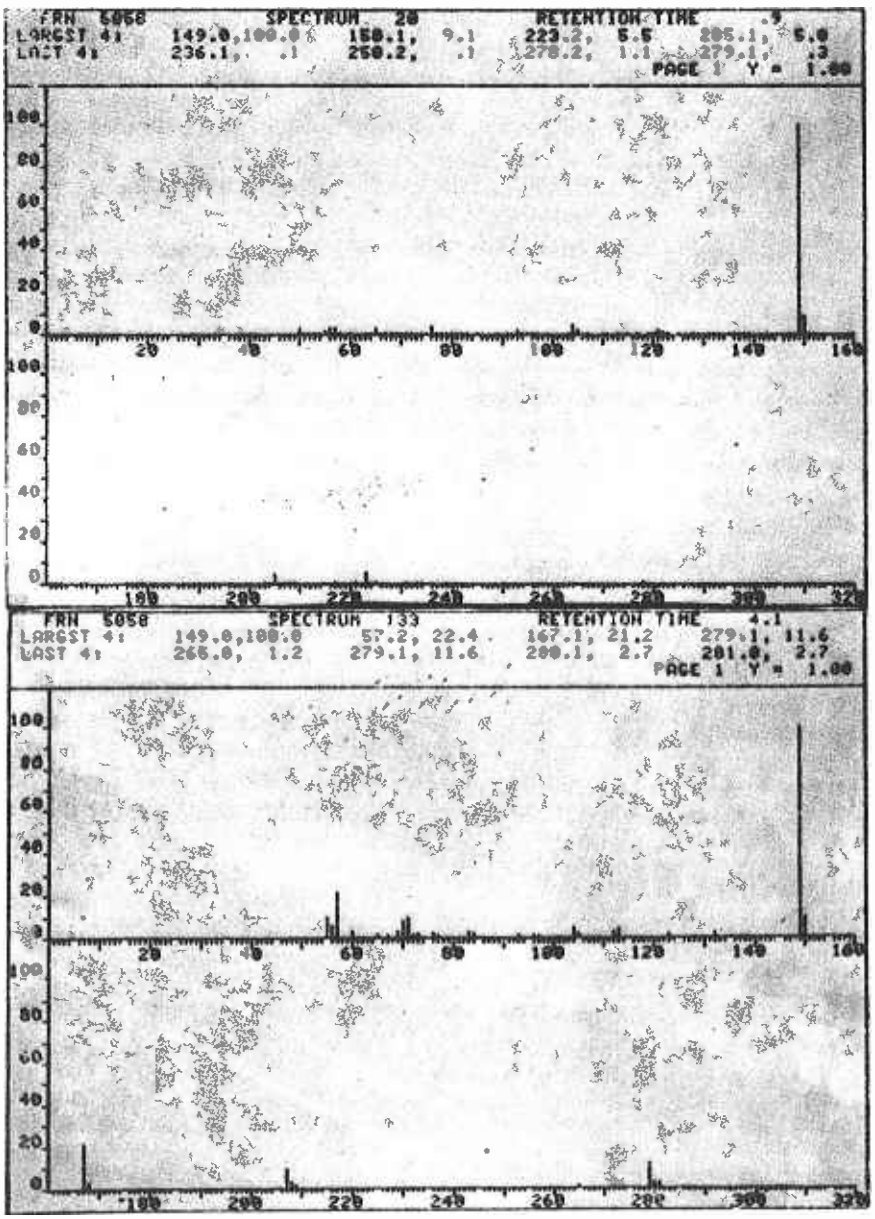
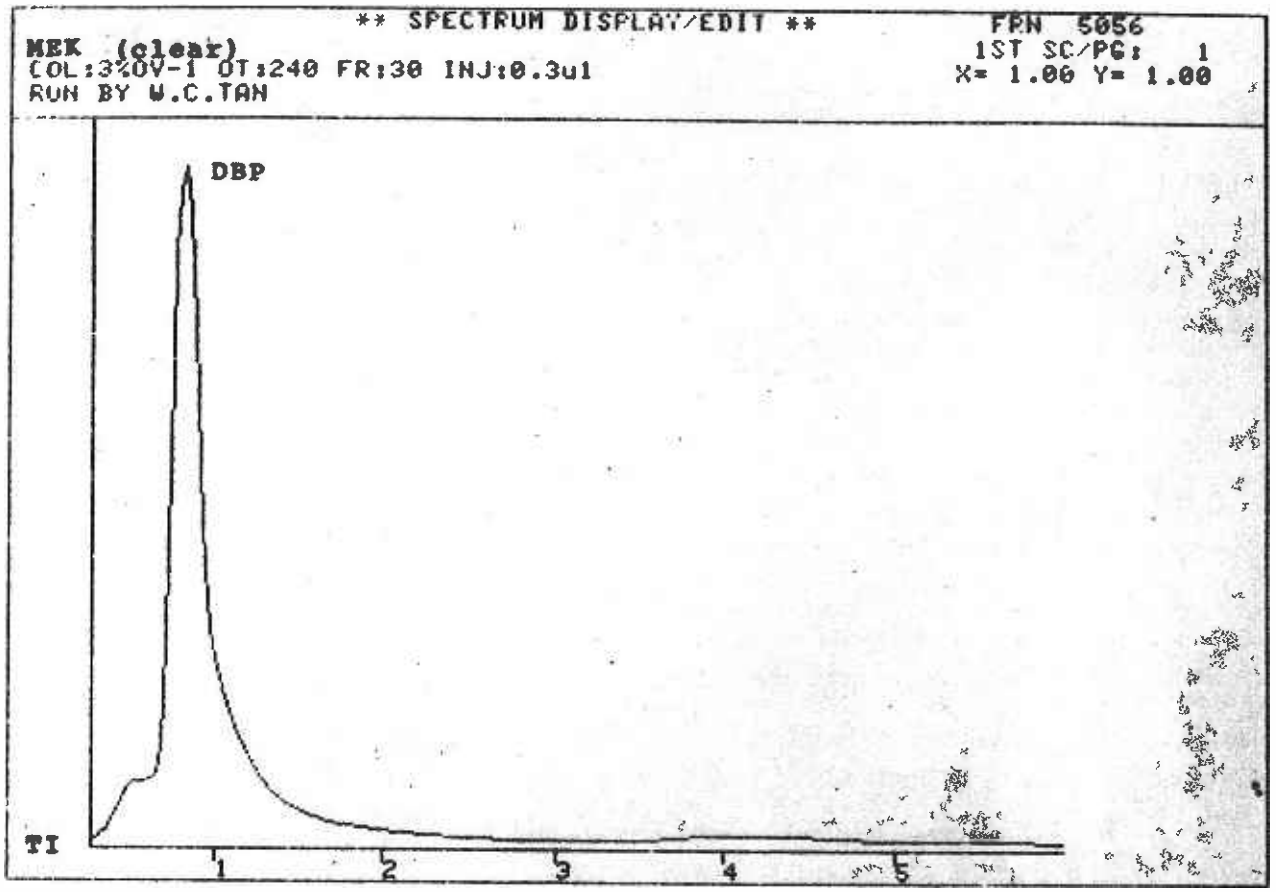


Figure 2 Total ion chromatogram and mass spectrograms of non-volatile residue from "cloudy" MEK.



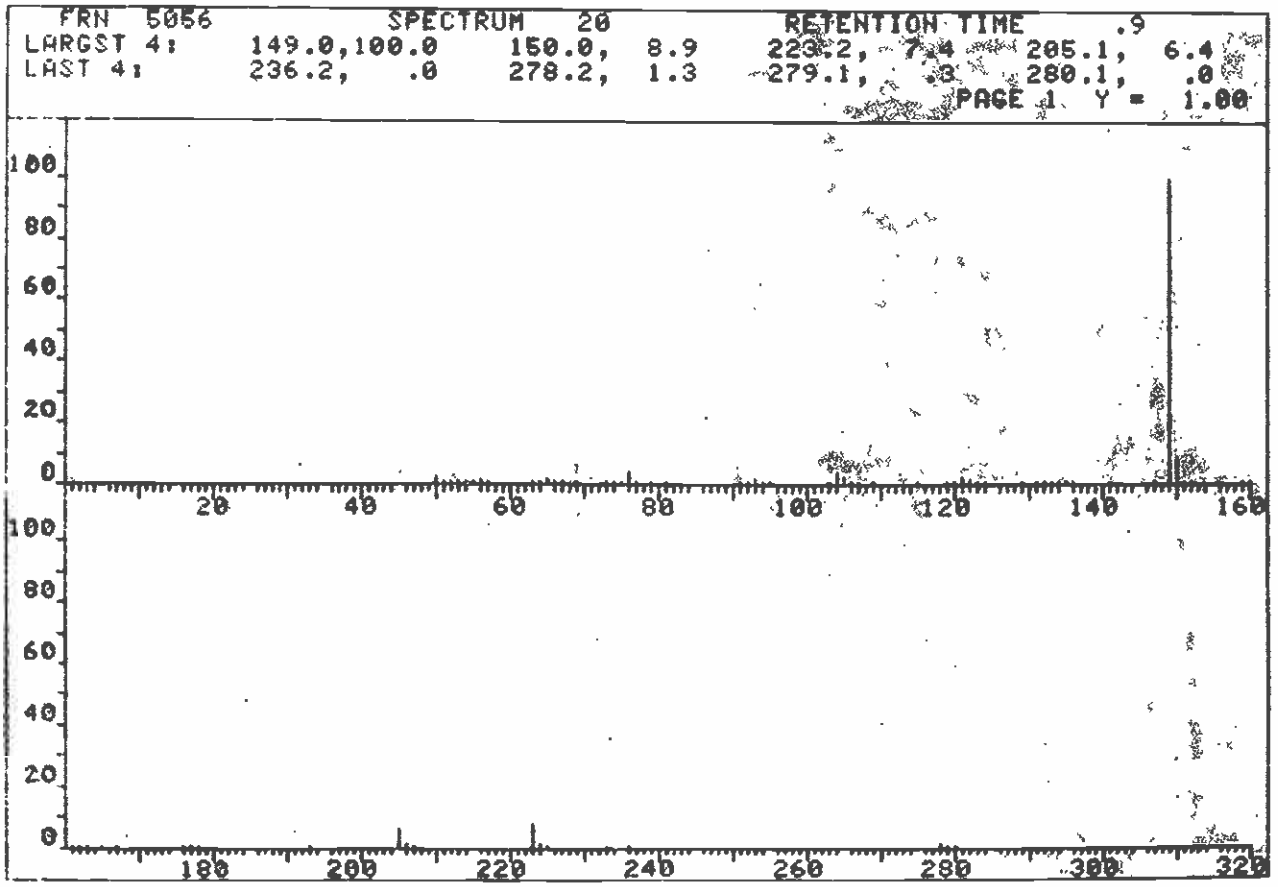
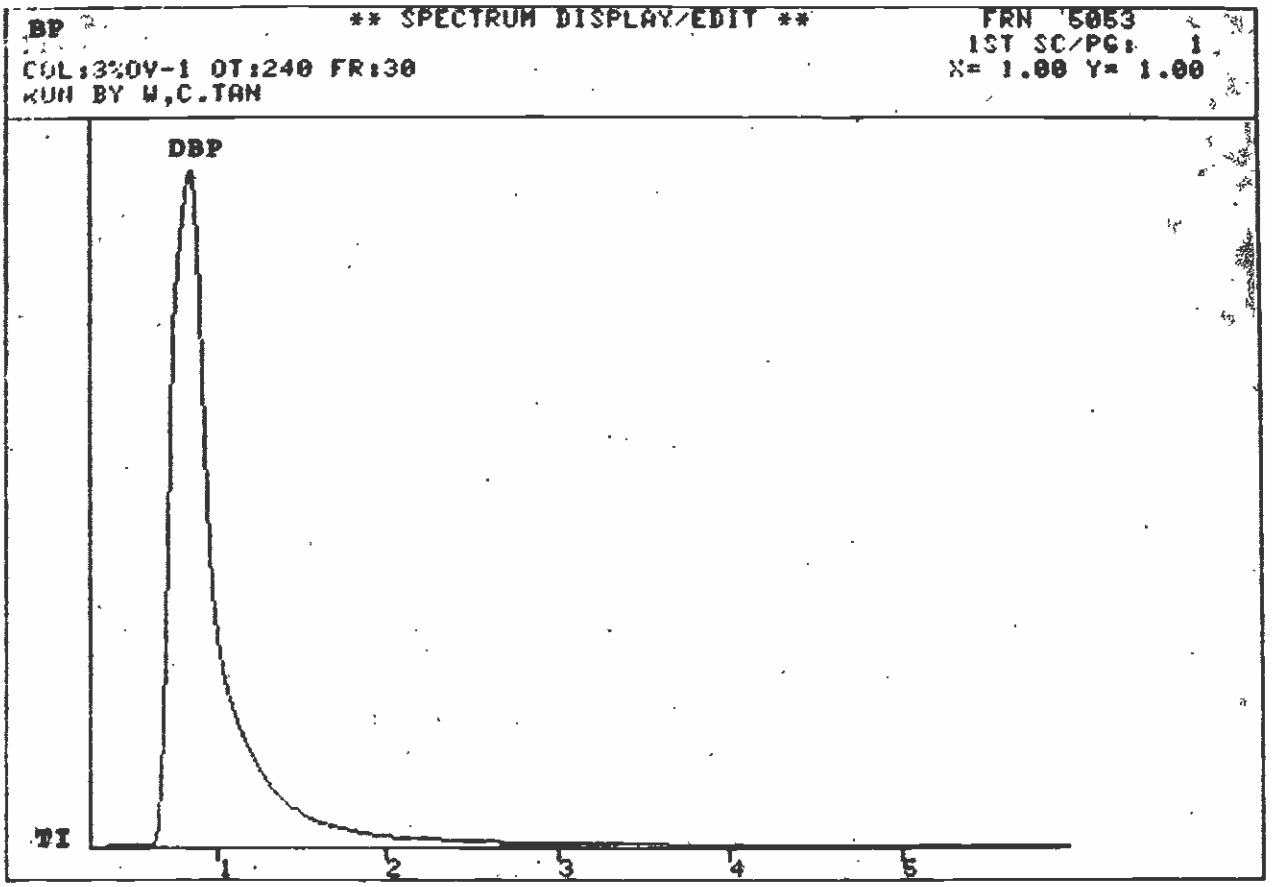


Figure 3 Total ion chromatogram and mass spectrogram of DBP.



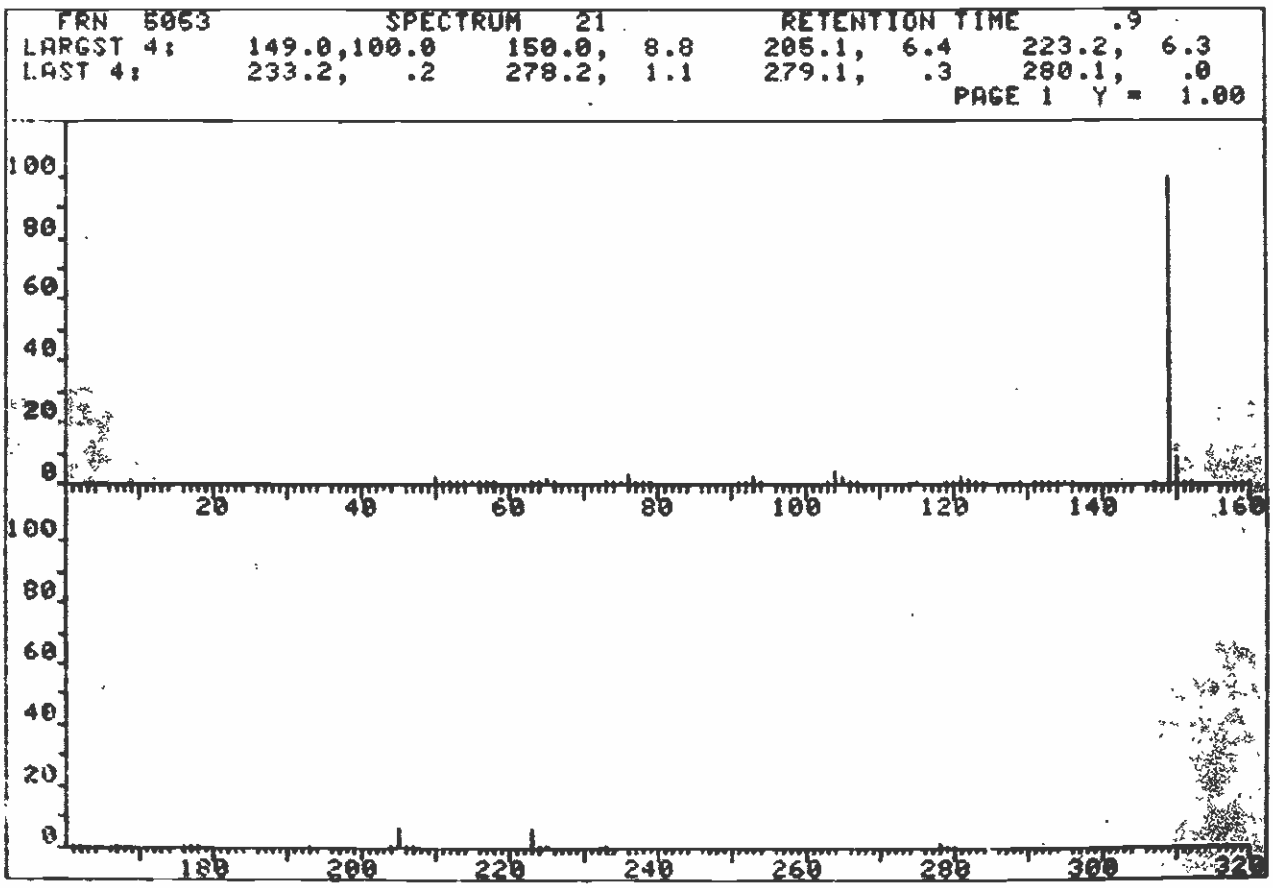
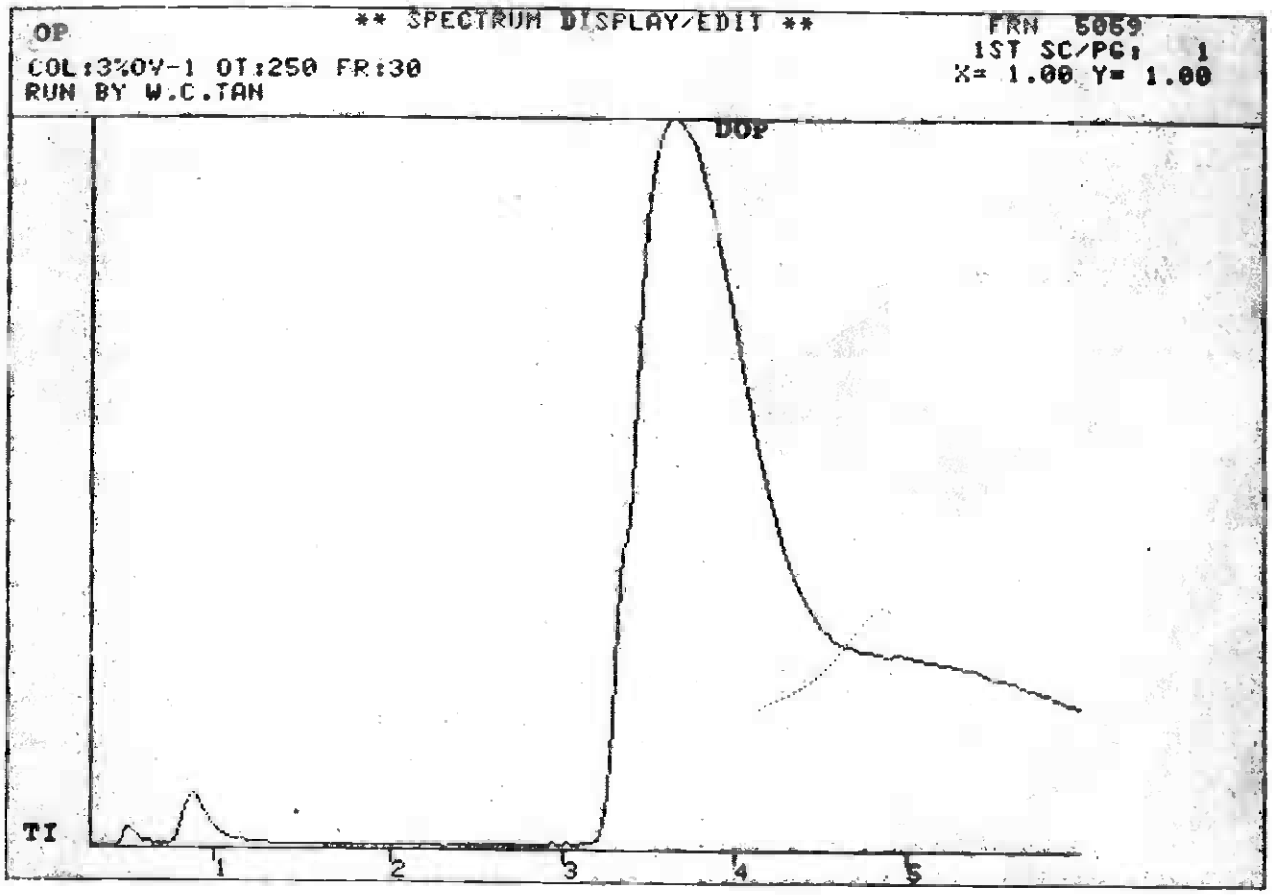


Figure 4 Total ion chromato gram and mass spectrogram of DBP.



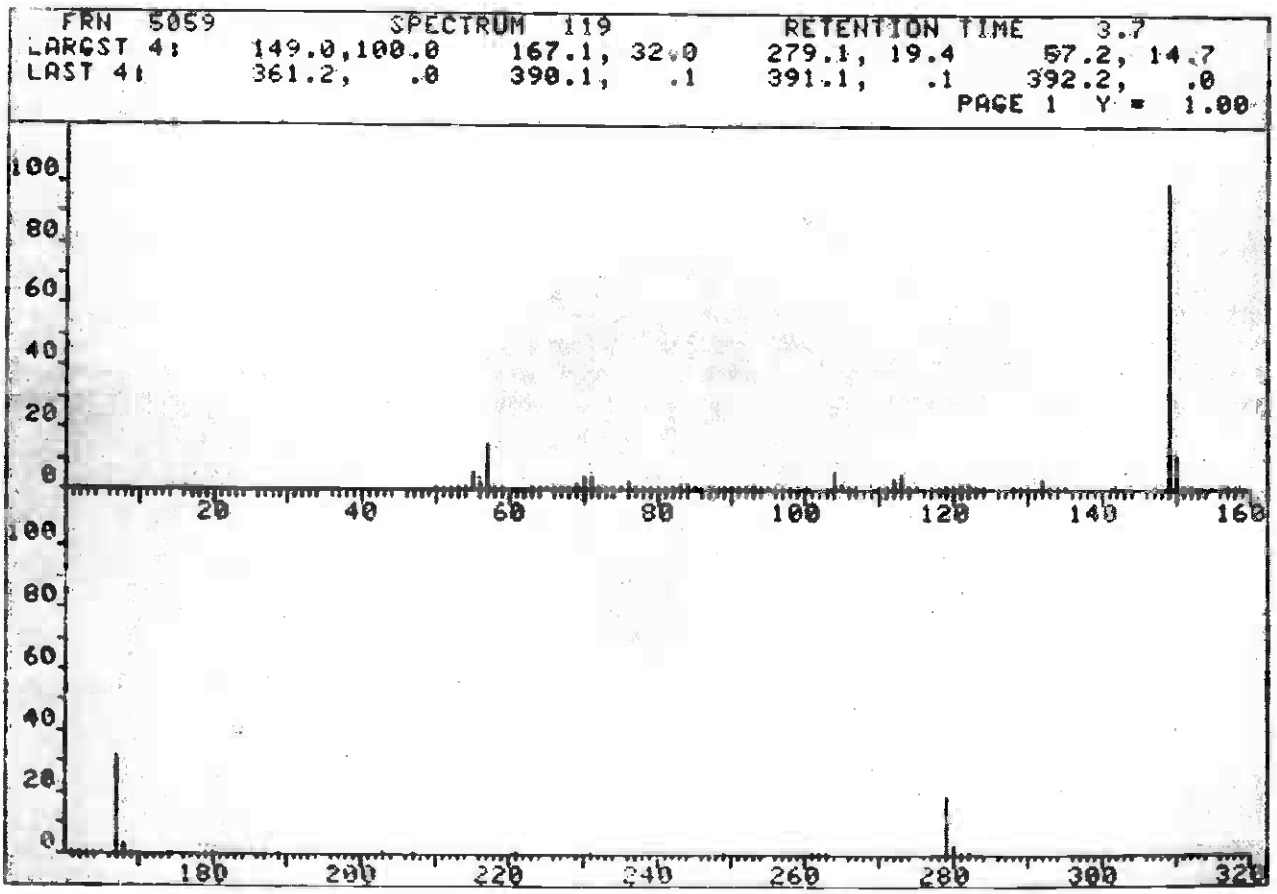


Figure 5 Total ion chromatogram and mass spectrogram of DOP.

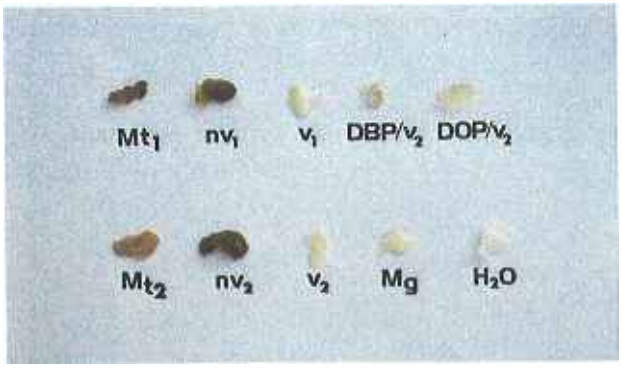


Figure 6 Some skin specimens from in vitro skin tests.

Mt_1 and Mt_2 : "Cloudy" and "Clear" MEK (drum) samples resp - red stain.

nv_1 and nv_2 : Non-volatile residues from "cloudy" and "clear" MEK resp - red stain.

v_1 and v_2 : Distillates from "cloudy" and "clear" MEK resp - no stain.

DBPv_2 : DBP in distillate of "clear" MEK - pink stain.

DOPv_2 : DOP in distillate of "clear" MEK - no stain.

Mg : MEK (GR grade) - no stain.

H_2O : Distilled water - no stain.

produce little irritant response (except perhaps for diallyl phthalate) when placed in contact with human skin (7). In his review, Fassett did not report any instance of sensitisation from phthalate esters (quoted by Lawrence) (8).

It is possible that the red staining observed clinically in our cases and produced in vitro by the MEK drum samples and resultant non-volatile residues were caused by certain phthalate contaminants, with DBP being a contributory component. Many of the commercially available phthalate esters contain impurities, including homologues and isomers (7). As only the drum samples of MEK were found to contain phthalate contaminants, it would appear that the source of the contamination could have been the drums. Apparently some of these drums were reconditioned ones previously containing DBP or DOP which were imported in such drums.

The variability in the amounts of phthalate contaminants from drum to drum may have accounted for the differences in the gross appearance of the different batches of MEK. The "cloudy" batches appeared to contain sufficient amounts of the contaminants to cause the red staining observed clinically.

It was interesting that while DBP in the distillate of MEK produced a pink staining of the skin in vitro, it did not cause any staining when used in distilled water or other solvents, such as IPA and EA. The role of MEK here is uncertain, although it is possible that the distillate may contain certain volatile contaminants (not detectable by our GC/MS experiments) with some ability to produce staining in the presence of DBP.

While the question of the toxicological importance of phthalates has yet to be resolved (9), dermal absorption of such compounds should be minimised. The factories concerned have been advised on measures to reduce skin contact of the workers and factory 'D' has been asked to ensure that drums intended for reuse are thoroughly cleaned.

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