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The composition of cetostearyl alcohol

Cetostearyl alcohol is a material widely used in the pharmaceutical industry as a component of creams, ointments and emulsifying waxes. Variations in the behaviour of cetostearyl alcohol in production processes led to determination of its hydrophilic-lipophilic character by the method of Greenwald, Brown & Fineman (1956). Different batches, when titrated with water, in a benzene dioxane system gave different cloud points, presumably as a result of variable composition.

Examination of the cetyl and stearyl alcohol contents by gas-liquid chromatography on a 5 ft, 5% OV17 column at 190°, showed no correlation with the cloud point. However in many batches the total cetyl plus stearyl alcohol content amounted to only 80–85% w/w of the total. Even if myristyl alcohol, another normal component, was included, the total was often still below 90%.

The British Pharmacopoeia monograph for cetostearyl alcohol contains a number of limit tests which control the quantities of other classes of compounds which could be present. Fatty acids are controlled by titration with 0·1 N sodium hydroxide to a limit of 0·14% w/w calculated as stearic acid. Esters are controlled by the Saponification Value to a limit of less than 0·01% w/w in terms of methyl stearate. Unsaturated components are controlled by the Iodine Value to a limit of 3% w/w in terms of oleoyl alcohol. However in our experience of this determination this value rarely exceeds the equivalent of 1% w/w. Hydrocarbons are controlled gravimetrically after a chromatographic separation on alumina; the limit corresponds to 1·5% w/w. Hydrocarbons are frequently present in commercial material at levels exceeding 1% w/w, however none of these components can account for the missing 10% of the total.

Examination of the gas chromatographic traces used for the analysis of the cetyl and stearyl alcohols revealed a number of extra peaks. To improve the resolution of these compounds a 13 ft 9% OV 101 column was specially constructed and used with temperature programming from 160° at 6° min^{-1} to 300° (Fig. 1). At higher sensitivity more components are detected. Peaks equivalent to more than 0·01% w/w of the mixture account for approximately 99% of the total. Thirty-six batches from five different suppliers were examined by this means. Components were identified initially by comparison of the retention times of the parent compounds and

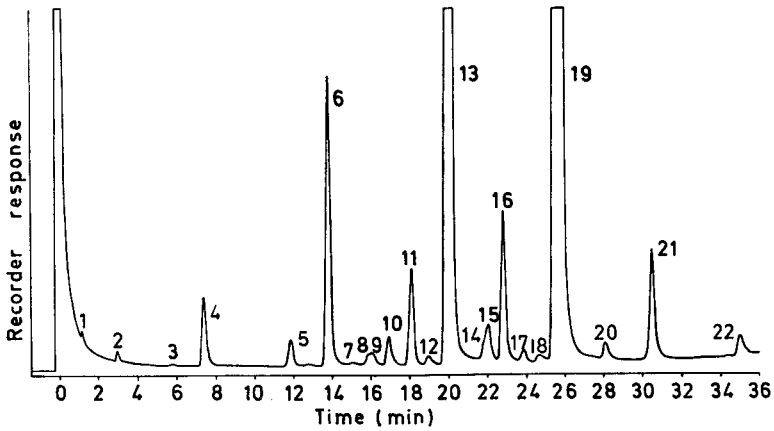

FIG. 1. Gas chromatographic separation of the components of commercial cetostearyl alcohol.

their silyl ethers with those of reference compounds. These identities were confirmed by gas chromatography-mass spectrometry and the components for which no standard substance could be obtained were also identified as far as possible by mass spectrometry. Additional use of the trimethylsilyl ethers on gas chromatography-mass spectrometry increased the relative abundance of M^+ and confirmed that all the alcohols contained a primary hydroxyl group, by giving a peak at $m/e = 103$ due to $CH_2{=}O^+ - SiMe_3$. Table 1 shows the composition of three typical batches from different suppliers received during 1973. The percentages are calculated with respect to the authentic substance, where this was available, and by comparison with the area of the nearest homologous authentic substance, where the compounds were not available.

All batches showed the same component profile although in widely varying amounts. The presence of the even numbered straight chain alcohols from C_8 to C_{22} was to be expected; they account for 90–95% of the total. In addition hydrocarbons were known to be present (*vide supra*) and these account for between 0·1 and 1·4% of the total (consisting principally of n-hexadecane and n-octadecane). More surprising was the presence of odd numbered straight chain alcohols in fairly large quantities, n-heptadecanol frequently being the fourth largest component. These may account for between 1 and 3·5% of the mixture. It is possible that these arise as a by-product in the reduction of fatty acids to alcohols in the manufacture of cetostearyl alcohol.

A further quantity of 0·2–2·0% of the mixture is attributable to various branched chain primary alcohols which may also arise from rearrangements occurring during reduction of the fatty acids. It was not possible to decide from the mass spectra the exact structure of these components.

Oleoyl alcohol could not be detected in the mixtures, possibly because although resolved from stearyl alcohol when present in equal quantities, it is swamped when a large excess of stearyl alcohol is present. Addition of a small quantity of bromine to the mixtures to produce dibromostearyl alcohol from the oleoyl alcohol resulted in a peak with a much longer retention time well resolved from all others. By comparison with dibromostearyl alcohol from standard oleoyl alcohol this was estimated to account for about 0·1% of the mixture.

It is interesting to note that there may have been an increase in the levels of the minor components over the last few years, since on re-examining batches which were received in 1967 and 1968 it was found that the cetyl plus stearyl alcohol content was usually over 95%.

Table 1. *Composition of batches of cetostearyl alcohol*

Peak	Identity	Percentage w/w 1	2	3
1	n-Octanol	0·02	0·06	0·07
2	n-Decanol	0·03	0·13	0·24
3	n-Tetradecane	—	0·01	0·01
4	n-Dodecanol	0·40	1·40	2·20
5	n-Hexadecane	0·03	0·38	0·25
6	n-Tetradecanol	4·10	3·20	3·60
7	n-Heptadecane	—	0·01	0·01
8	Pentadecanol* †	0·12	0·49	0·37
9	Pentadecanol* †			
10	n-Pentadecanol	0·20	0·62	0·56
11	n-Octadecane	0·09	1·05	0·75
12	Hexadecanol*	0·05	0·14	0·17
13	n-Hexadecanol	24·50	25·40	24·90
14	Heptadecanol* †	0·31	0·88	1·15
15	Heptadecanol* †			
16	n-Heptadecanol	1·31	2·12	2·30
17	Octadecanol*	—	0·15	0·15
18	Octadecanol*	0·04	0·15	0·10
19	n-Octadecanol	65·10	61·10	58·20
20	n-Nonadecanol	0·08	0·33	0·34
21	n-Eicosanol	0·57	1·70	1·83
22	n-Decosanol	0·05	0·35	0·44

* Branched chain primary alcohols.
† Incompletely resolved.

A Pye 104 chromatograph with flame ionization detector was used. The glass columns were packed with the appropriate stationary phase (OV17 or OV101) coated on Gas-Chrom Q (acid washed and silanized) (80–100 U.S. mesh). Columns were operated with a nitrogen flow of 40 ml min^{-1} and the injection heater on + 5. For mass spectrometry, an A.E.I. M.S. — 30 Double beam, double focusing instrument was used.

Standard substances, which were all better than 99% pure, were obtained as follows: n-octanol from Fisons Scientific Apparatus Ltd., n-dodecanol, n-hexadecanol n-octadecanol and n-octadecane from BDH Chemicals Ltd., n-decanol, n-tetradecanol n-eicosanol, n-docosanol, n-hexadecane and n-eicosane from Koch-Light Laboratories Ltd. To prepare silyl ethers, 100 mg of cetostearyl alcohol was dissolved in 0·5 ml of pyridine and 0·5 ml bis-(trimethylsilyl) acetamide. The mixture was heated to 50° for 10 min.

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