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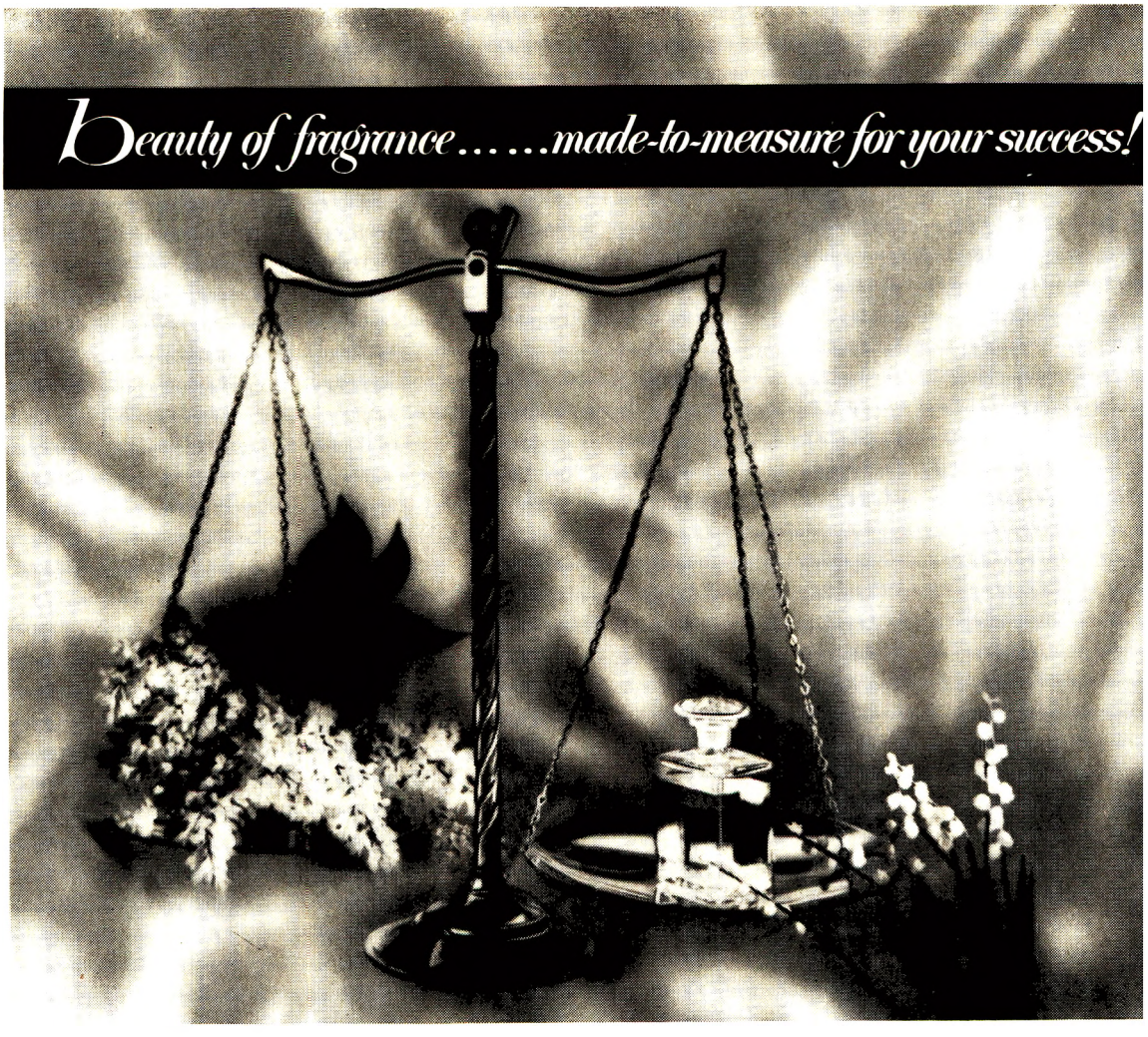

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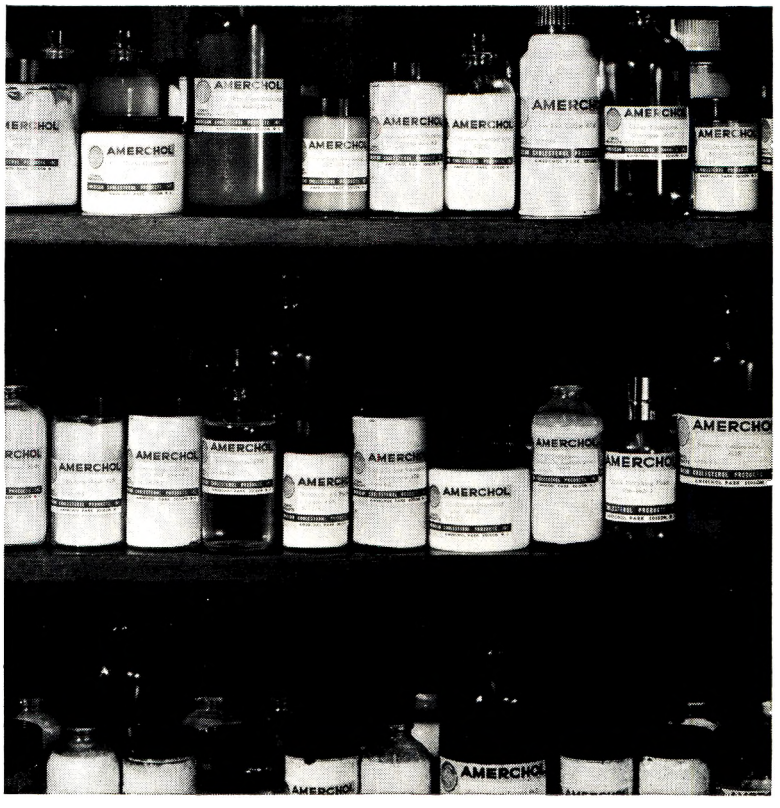

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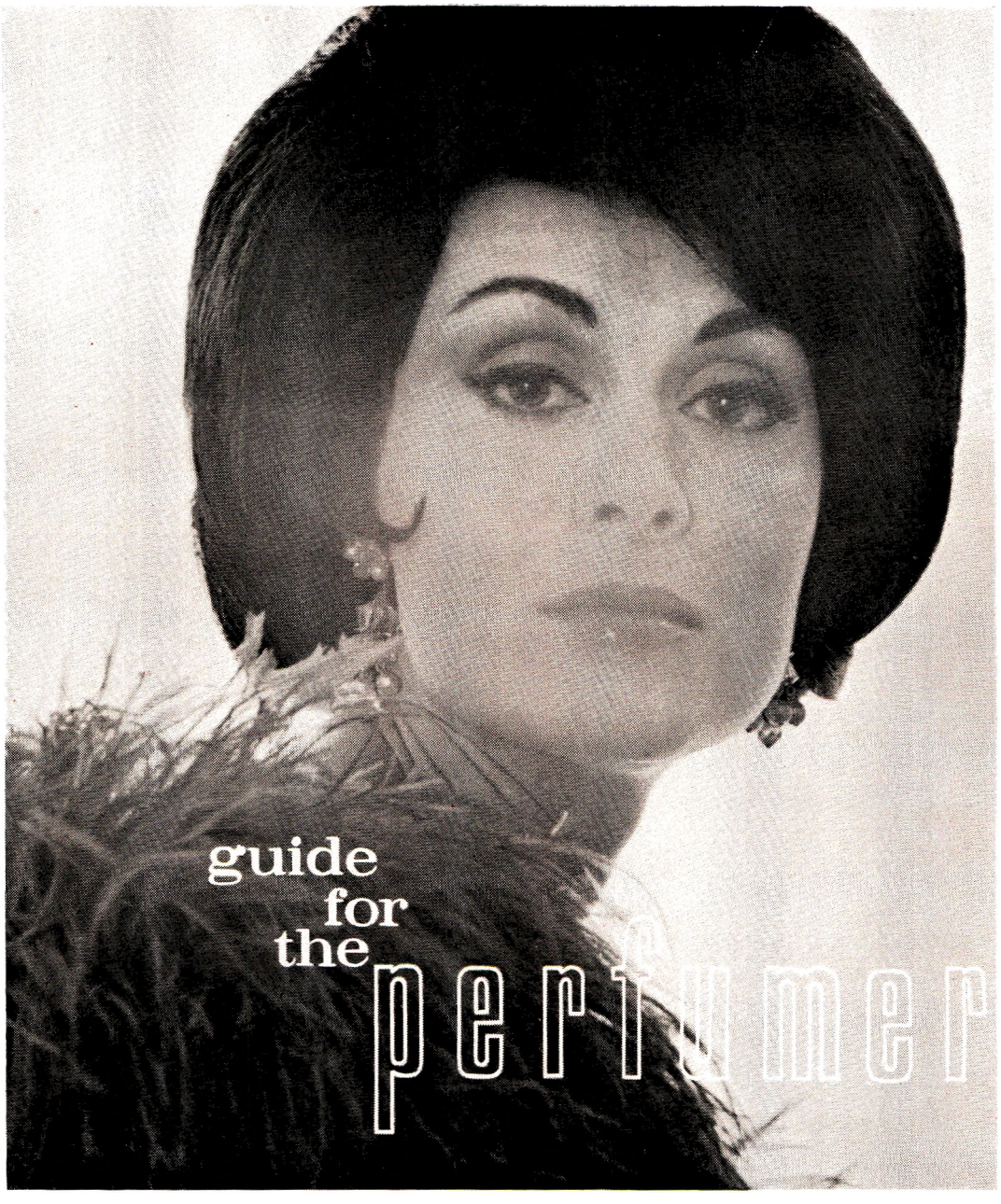

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SYNOPSES FOR CARD INDEXES

The following synopses can be cut out and mounted on 5″ × 3″ index cards for reference without mutilating the pages of the Journal.

The preservation of shampoos: D. M. BRYCE and R. SMART.
Journal of the Society of Cosmetic Chemists **16** 187-201 (1965)

Synopsis—Evidence is presented that difficulty is experienced in shampoo preservation, due to the effect of micellar solubilisation.

The nature of the preservative requirement is discussed and performance of phenyl mercuric nitrate and formaldehyde briefly examined.

Bronopol, a new preservative, which is active in the presence of anionic and nonionic surfactant micelles, appears to have application in this field.

Measurement and prevention of oxidative deterioration in cosmetics and pharmaceuticals: J. P. OSTENDORF.
Journal of the Society of Cosmetic Chemists **16** 203-220 (1965)

Synopsis—Oxidation mechanism, and the factors that are responsible for the initiation of oxidation are reviewed. The various methods with which the oxidation can be traced are mentioned. With this knowledge in mind the prevention of oxidation is reviewed. First the mechanism, then the various general precautions to be taken, and the antioxidants. Examples are cited.

Protection of the pack and its contents against UV light: A. R. BROWN.
Journal of the Society of Cosmetic Chemists **16** 221-236 (1965)

Synopsis—The life and value of plastics packaging materials are increased by incorporating additives which protect them from the damaging effects of the ultra violet radiation present in natural and artificial light. The theoretical background is given with a review of the commercial ultra violet absorbers available for plastics use in the packaging of cosmetics.

Journal of the Society of Cosmetic Chemists

This edition is published for

THE SOCIETY OF COSMETIC CHEMISTS
OF GREAT BRITAIN

by Pergamon Press, Ltd., Headington Hill Hall, Oxford

Editorial Office : Ashbourne House, Alberon Gardens, London, N.W.11.

VOL. XVI 1 APRIL 1965 No. 4

GENERAL NOTICES

Publication dates: The "Journal of the Society of Cosmetic Chemists" is published every four weeks.
Five issues for the Society of Cosmetic Chemists of Great Britain by Pergamon Press Ltd., Headington Hill Hall, Oxford, England.
Six issues by the Society of Cosmetic Chemists from 201 Tabor Road, Morris Plains, N.J., U.S.A.
Two issues by the Gesellschaft Deutscher Kosmetik-Chemiker, e.V. from Hamburg-Grossflottbek, Beselerstrasse 1, Germany.

Issue No.	*Publication Date*	*Country of Origin*
1	8th January	Great Britain
2	5th February	U.S.A.
3	4th March	U.S.A.
4	1st April	Great Britain
5	29th April	Germany
6	27th May	U.S.A.
7	24th June	Great Britain
8	22nd July	Great Britain
9	19th August	U.S.A.
10	16th September	U.S.A.
11	14th October	Great Britain
12	11th November	Germany
13	9th December	U.S.A.

Advertisements : All enquiries regarding advertisements in the British Editions of the Journal should be addressed to Mr. J. V. Robinson, Pergamon Press, Ltd., 4 & 5 Fitzroy Square, London, W.1.

Subscription : All members of the Society of Cosmetic Chemists of Great Britain receive one copy of each edition free. Further copies at non-member rates. Non-members: £10 per annum, post free, or £1 per issue, post free.

Missing Numbers : **Journals are despatched at Printed Paper rate. Claims for missing numbers can be entertained only from subscribers in the country of origin of the particular issue, and must be made within 30 days from date of issue.** Members and subscribers are urged to give notice of change of address to the Publication Offices.

Responsibility for statements published : The Society of Cosmetic Chemists of Great Britain and its Hon. Editor assume no responsibility for statement or opinions advanced by contributors to this Journal.

Lectures : The Society shall have the right of first publication of any lecture or address delivered before it, but does not undertake to publish any given matter.

Manuscripts : These should be in accordance with the "Directions for Preparation of Manuscripts," copies of which are available from the Hon. Editor, Ashbourne House, Alberon Gardens, London, N.W.11.

J. Soc. Cosmetic Chemists **16** 187-201 (1965)

The Preservation of Shampoos

D. M. BRYCE and R. SMART*

Presented at the Symposium on "Preservatives and Antioxidants", organised by the Pharmaceutical Society of Great Britain and the Society of Cosmetic Chemists of Great Britain, in London on 17th November 1964.

Synopsis—Evidence is presented that difficulty is experienced in shampoo preservation, due to the effect of micellar solubilisation.

The nature of the preservative requirement is discussed and performance of phenyl mercuric nitrate and formaldehyde briefly examined.

Bronopol, a new preservative, which is active in the presence of anionic and nonionic surfactant micelles, appears to have application in this field.

Introduction

The job facing the manufacturer of shampoo is no different from that facing the manufacturer of any other type of cosmetic preparation, namely, presentation at the point of sale of a physically and chemically stable, hygienic, product.

As it is probable that 90% or thereabouts of shampoo sold in this country is based on the detergent action of sulphated lauryl alcohols and ethers, and as these are widely and rightly believed to be antagonistic to bacterial and fungal growth, it might be supposed that no problem of a hygienic or preservative nature would be likely to arise in formulation. Such is not, however, the case as reference to the literature readily demonstrates.

McCulloch (1), for example, particularly refers to the paper by Baker *et al* (2) who found that all anionic detergents included in their studies, mostly alkyl sulphates, selectively inhibit the metabolism of gram-positive micro-organisms. None of the anionic detergents at a concentration of 0.1% was effective against any of the three gram-negative organisms tested.

*Boots Pure Drug Co. Ltd., Nottingham.

He also refers to his own work showing that triethanolamine lauryl sulphate is selectively bactericidal against gram-positive organisms.

Schwartz and Perry (3) again quote Baker *et al* (2) and later (4) they say that it is now very well established that many anionic detergents are powerful bactericides, in some cases rivalling the best cationics. In general, however, the anionics tend to have a narrower bactericidal field than the cationics, and their action is influenced to a much greater extent by changes in pH.

Despite such warnings, commercial products are not infrequently encountered that give high microbial counts, which perhaps illustrates both the inherent difficulty and, in certain cases, even the lack of appreciation of the preservative problem.

The Occurrence of Micro-organisms in Shampoo

The figures in *Table I*, taken from our records of examinations of proprietary shampoos, indicate the extent of bacterial contamination that can be found.

Table I

Type of shampoo	Number of bacteria per gram
Liquid, various brands	15000, 70000, 100000, 10^6.
Liquid, medicated, various	1400, 15000, 13000, 3×10^7, 60000, 280000
Liquid, beer	6×10^6
Liquid, milk	10^7
Liquid, egg and lemon	1.1×10^7
Cream conditioner	10^6

Where large numbers of organisms were present, they were without exception gram-negative staining, non-sporebearing rods. Several of these were pseudomonads. Less frequently, sporebearing, aerobic bacteria were found–but these were usually present in smaller numbers.

In many cases the contaminants were isolated, and added to our collection of cultures of useful organisms. This collection plays an important part in any subsequent test of preservative activity in shampoo and related formulations.

We have seldom encountered heavy yeast or mould infection in this group of products although such does occur more frequently, we believe, particularly in warmer parts of the world. In this sense it is possible that our experience is atypical as Wilkinson *et al* (5) write "most modern shampoo materials are liable to mould attack unless preserved with

materials like hydroxybenzoate esters," which suggests some first-hand experience of the matter.

The Consequences of Microbiological Infection

The consequences, to the product, of heavy growths of micro-organisms are likely to be deterioration in odour of the shampoo, perhaps accompanied by physical change such as formation of a turbidity or deposit, or change in flow properties; but such is by no means invariably the case. We have not infrequently seen material containing 10^6–10^7 organisms/g that showed no obvious sign of deterioration. Few would disagree that such material is nevertheless unfit for sale.

Consequences to the user arising from the presence of heavy organic growth appear to be unlikely, but there is, at least, a theoretical risk.

General Considerations About Preservation

It is difficult to know how far one can usefully generalise in dealing with a matter like preservation. Preservation problems tend to be individual problems with individual solutions—owing to the many contingent variables represented by formula, pack, conditions, and method of manufacture and distribution. The magnitude of such problems varies widely in different cases.

It may be useful to examine, in somewhat greater detail, these significant factors, the interplay of which will decide the satisfactory performance and nature of product or otherwise.

They can be considered under three main headings :—

(1) The microbiological challenge.

(2) The manufacturing process.

(3) The product.

The Microbiological Challenge

Aseptic conditions of manufacture and packaging are neither economic nor necessary for a product of this type. There will therefore be a microbiological challenge to the product, the magnitude and quality of which will vary with the state of the ingredients and water supply, the level of factory hygiene, and the season.

The number of organisms present from the above sources has a very great bearing on their subsequent ability to proliferate in the shampoo. Very small inocula have little opportunity to multiply, on account of the multiplicity of adverse environmental factors that operate during the

manufacture of a shampoo. The actual safe limit in any particular case is difficult to determine, but in our experience the presence of thousands of organisms/ml (or swab) is definitely suspect, and calls for remedial action ; hundreds are treated with reserve, but tens may be unavoidable although zero counts can be obtained regularly where processes are satisfactorily controlled.

Water supply is particularly important, and whether derived from public mains, still or demineraliser, it is sound practice that its microbiological state should be monitored, particular attention being paid to the state of pipework, valves and hoses, loops and other sites of water stagnation. These may be storage tank level indicators or redundant or seldom used branch lines or valves.

Water from the public main usually contains no more than a few bacteria per ml, even after passing through factory pipelines and valves. Without adequate control, however, both tap water and purified water can issue from a valve or hose with a content of many thousands of pseudomonads and assorted gram-negative rods—an ample inoculum for trouble!

Ingredients can, of course, prove a potent source of contamination. As active bacterial proliferation has been observed on one occasion in a 25% solution of sodium diethoxylauryl sulphate (6) they merit serious attention. Although such a case may well be exceptional, it is most important that both the shampoo manufacturer and the basic material manufacturer take adequate steps to ensure that no build up of resistant organisms occurs in their storage and distributive systems. This is effected by careful factory and warehouse hygiene with steaming or formalin treatment of containers, tanks and pipes as necessary. It is a practice of the trade to add preservative to raw materials the self-preserving abilities of which are in any way suspect.

Factory hygiene is a subject in itself (7), for at all stages of manufacture it is clearly vital to take adequate steps to maintain the cleanliness of factory plant. Treatment of bottles, caps and cap liners also merits consideration under this heading.

The Manufacturing Process

Particular aspects of the manufacturing process relevant to preservation, apart from the general state of hygiene of plant, storage tanks and pipework, which has been noted above, are the presence or absence of heating operations or warm storage.

Manufacture of liquid shampoo does not, in general, necessitate a microbiologically effective heating stage, but where such is present it is clear that a useful product safeguard exists. On the other hand, to hold bulk material under warm conditions for any length of time can be equally disastrous if a significant inoculum of resistant organisms is present. (Many *pseudomonads* have an optimum growth temperature of 25°C or even lower.) The scale of manufacture therefore has a direct bearing on preservation.

The Product

To some this might appear to be the only proper subject for consideration in the context of preservation. It is certainly the most obvious source of variables, of which the following come to mind :

(a) The nature and amount of shampoo ingredients. Ultimately, osmotic pressure may be expected to guarantee the integrity of a preparation. As a possible example, our company has for many years sold a shampoo containing 36% of active matter with 10% propylene glycol. This has never provided a preservative problem–nor is it likely to.

(b) Presence or otherwise of nutritious material, e.g. beer, milk, amino acid, or other nitrogenous components.

(c) Presence of medicaments may be beneficial, but may also give rise to a false sense of security. It is necessary to bear in mind that few cosmetically acceptable bactericides are particularly active against pseudomonads even in the absence of surfactant micelles.

(d) Perfume.

(e) Inactivators, e.g. lecithin and nonionic surfactant.

(f) pH can in itself be most discouraging to micro-organisms.
The normal pH range of liquid shampoos is 6 to 8, although cream shampoos containing a significant amount of soap may run up to about pH 9.
Within these limits the effect of pH will be felt mainly by its action on the surfactant, the antibacterial performance of anionic detergents rapidly improving as the pH moves to the acid side.

(g) Of added preservative we would only say here that its presence is essential unless the inherent resistance of the product is very high.

(h) Under this heading, too, we should make clear that we include the

pack with all its implications for the formula, such as light transmission characteristics, reactivity and mass transfer effects.

It is well known, for example, that perfume ingredients readily migrate to polythene, but it is also true that low density bottles can pick up a substantial amount of fatty matter, the amount rising markedly with temperature up to perhaps 1% of the weight of polythene at 60°C. We would add that we have also noted a significant uptake of methyl hydroxybenzoate in certain cases, and propyl hydroxybenzoate can be rapidly lost at higher temperatures, e.g. 25% at 45° and 50% or more at 60°C.

Methods of Assessment

The interplay of three sets of factors then will decide the eventual microbiological condition of a manufactured product, and although we have some measure of control over all of them, control is clearly minimal in the case of the microbiological inoculum. It is apparent that the preservative ability of the product should be well in excess of the necessary minimum to inhibit the anticipated flora, and ideally one aims for a product that is sterile. On the other hand, the use of excessive amounts of preservative may result in a product that is unacceptable to the user or the dermatologist. Unfortunately there is no simple and conclusive test for *adequacy* of preservation. It is only possible to make an assessment from laboratory tests carried out on laboratory or factory-made material. The weight and worth of the assessment will vary with the amount of experimental work on which it is based, for example, the range of conditions explored, the numbers and types of organisms used, and the length of the period of observation. It must always be accepted that unforeseen and exceptional organisms or conditions may turn up during routine manufacture and packaging of the material to vitiate the conclusion.

Within this framework, a number of experimental approaches may be made and it is our practice to heavily inoculate a series of samples with a number of mixed cultures of bacteria, yeasts or moulds. After inoculation the samples are stored at 25°C, and the fate of the organisms is followed by culturing aliquot samples on nutrient media at the same temperature at regular intervals. If at any time there is an immediate decrease to zero counts which are maintained for a few weeks, a second challenging inoculum is added with further periodic culturing. This provides information on the sustained ability of the preservative to protect the product, i.e. stability. Resistant organisms obtained from contaminated shampoos

are always included in these tests and also in any tests of inhibitory concentrations of preservatives proposed for shampoo formulations.

Preservatives Used

Excepting those few cases where the preparation is self preserving it is essential to incorporate an effective preservative, the basic requirements of which are a wide range of antimicrobial activity together with acceptable toxicity at the use concentration. It is desirable that it should also be inexpensive, colourless, odourless and stable, which brings us to the difficulties peculiar to shampoos. The physical state of high concentrations of surfactant is such that the main armament of phenolic and similar preservatives, like benzyl alcohol or benzoic acid, are of little use at normal levels of concentration and pH, and we find a very restricted list of possible candidates for the job.

Organic mercurials

These compounds, particularly phenyl mercuric acetate, borate and nitrate are sometimes recommended (13), although higher concentrations are necessary than would be used in simpler contexts. There is, however, a possibility of loss of activity at higher pH, and in the presence of halide ions, which is a serious objection in view of the common use of salt for thickening purposes. Indeed phenyl mercuric salts may be regarded as cation active and liable to complexing with anionic surfactant in the same manner as the more frequently encountered quaternary salts. Decomposition in the presence of aluminium is a minor matter by comparison but not irrelevant.

To demonstrate the effect of two common shampoo bases (*Empicol TLP** and *Empicol ESB***) on the stability of phenyl mercuric nitrate (PMN), a series of solutions at concentrations of 40% and 30% respectively, all containing 50 ppm PMN, were stored in the dark at temperatures of 30°C and 45°C. The activity of the PMN was estimated microbiologically by agar diffusion assay with large plates and *Bacillus pumilus* as test organism, a modification of the technique of Carter and Sykes (8) being used.

The results expressed as a percentage of the activity of a control solution at pH 5.5, kept at 0–4°C (normal refrigerator temperature) are given in *Table II*.

---

*38% triethanolamine lauryl sulphate with 1% alkylolamide.

**27% sodium diethoxylauryl sulphate.

Table II
Phenyl mercuric nitrate assays

30% *ESB3*	pH 5.5			pH 8.0		
Storage period	0–4°C	30°C	45°C	0–4°C	30°C	45°C
1 hour	100			104		
1 week	100	97	88	103	95	73
4 weeks	100	92	93	110	65	56

40% *TLP*	pH 5.5			pH 8.0		
Storage period	0–4°C	30°C	45°C	0–4°C	30°C	45°C
1 hour	100			111		
1 week	100	80	60	84 78*	38	(<20)
4 weeks	100	59	(<20)	57 63*	(<20)	(<20)

( )—result seriously affected by shampoo base activity below about 20%.
*—duplicate assay.

The lauryl ether sulphate showed no significant loss of activity over a 4 weeks' period at pH 5.5 at any temperature, but storage at pH 8.0 resulted in a 50% loss at 45°C. The triethanolamine lauryl sulphate solutions deteriorated much more rapidly at both pH values.

It is a further disadvantage of this group of preservatives that the medical profession tends to regard them with some suspicion, although we note that the Eurotox committee specifically approves the use of phenyl mercuric salts in shampoos, within certain concentration limits which are not specified (9).

They are, however, used in shampoos, and are occasionally declared as active ingredients.

Formaldehyde

The only really noteworthy preservative is formaldehyde, and despite the statement in Harry (10) that it is never used in toilet preparations it is in fact in widespread use, and is approved by the Eurotox committee in concentrations up to 0.05%.

It may be that this concentration is inadequate in certain contexts. Marchon, in their trade literature, for instance, recommend 0.08% (13) and General Mills (12) about the same, but it has been our experience that addition of 0.02% HCHO is sufficient in conjunction with adequate factory control.

The disadvantages of formaldehyde are obvious. It is volatile, odorous, reactive and liable to polymerize so that, at best, it disappears in course of time, at worst it reacts with some ingredient, such as the perfume or the colouring matter.

As a preservative it is highly active against both vegetative and sporing organisms, activity increasing rapidly with rising temperature. It has been stated to be almost inactive under 10°C. Its activity towards a range of bacteria including some shampoo contaminants in the presence of lauryl sulphate and lauryl ether sulphate is illustrated by a radial cup test. Cultures of the organisms were streaked radially from test solutions in 15 mm cups in a nutrient agar plate. Inhibition distances were measured after 24 hr incubation at 37°C.

Table III

Radial Cup Tests—mm inhibition from 15 mm cup.

Test material	*S. aureus*	*Strep. faecalis*	G–B (S)	*E.coli* (N.C.T.C. 86)	Ps.pyo. (B)	G–B (M)
ESB3 (30% in water)	7	5	0	0	0	0
,, + 0.1% formalin	7	5½	0	2½	1½	0
,, + 0.2% ,,	10	8	6	6½	3	1
TLP (40% in water)	7	7	0	0	0	2
,, + 0.1% formalin	8	8	½	4	1½	1½
,, + 0.2% ,,	11	10	7	7	3½	2

The superior activity of the shampoo bases towards gram-positive bacteria is clearly shown in *Table III*. The addition of formalin increased the range of activity on nutrient agar to include gram-negative organisms, three of which (S,B, and M) were resistant shampoo contaminants. This test, however, only detects inhibitory action in the presence of nutrient agar, and lethal tests (in which the organisms are inoculated directly into the solution to be tested and sampled at intervals into agar) showed that the *TLP* base had lethal activity towards the *Escherichia coli N.C.T.C. No. 86*, whereas the *ESB* had not.

Loss of formaldehyde from a shampoo can readily be followed by chemical assay, and varies with the reactivity of the system. The experimental results in *Table IV* show the sort of loss to be expected in contact with a simple shampoo base. Losses in a finished shampoo containing other potentially reactive components would be expected, in general, to be greater.

Table IV

Formaldehyde assays

Loss of formaldehyde, after storage under various conditions at the specified temperatures, from basic shampoo solutions to which formalin has been added at the indicated rates.

0°C	40% *TLP*		30% *ESB3*	
	pH 5.5	pH 8.0	pH 5.5	pH 8.0
Formalin addition %	0.05	0.05	0.05	0.05
10 weeks	0.016	0.019	0.017	0.018

30°C	40% *TLP*				30% *ESB3*			
	pH 5.5		pH 8.0		pH 5.5		pH 8.0	
Formalin addition %	0.05	0.12	0.05	0.12	0.05	0.12	0.05	0.12
1 week	0.022	0.046	0.023	0.054	0.019	0.059	0.022	0.061
7 weeks	0.020	0.045	0.012	0.032	0.019	0.050	0.022	0.055
10 weeks	0.015	0.036	0.006	0.020	0.012	0.039	0.016	0.045

45°C	40% *TLP*		30% *ESB3*	
	pH 5.5	pH 8.0	pH 5.5	pH 8.0
Formalin addition %	0.12	0.12	0.12	0.12
10 weeks	0.031	nil	0.046	0.041

Results expressed as % HCHO w/v

Bronopol

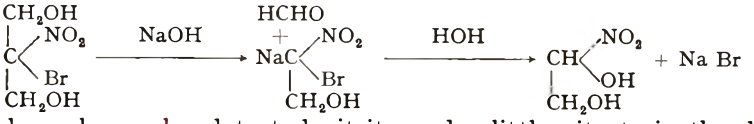
In circumstances where formaldehyde is contraindicated for reasons of incompatibility, we have made successful use of a product of our own research laboratories, 2-bromo-2-nitropropane 1,3-diol. (Approved name : *Bronopol.*) Despite instability in alkaline solution, and in the presence of sunlight, we have been able to solve a number of preservative problems with its aid and have found as little as 0.01% adequately preservative in certain cases.

A preliminary account of its properties has been published by Croshaw *et al* (11).

It is a colourless, virtually odourless, crystalline solid, highly soluble in water (about 25%), very slightly soluble in oil (<0.5%), with a wide spectrum of antibacterial activity.

It is reasonably stable in acid solution in the absence of sunlight, but is readily hydrolysed under alkaline conditions with formation of formaldehyde.

Breakdown may occur along the following lines



although we have also detected nitrite and a little nitrate in the decomposition products.

Degradation can be followed by assay of HCHO or bromide liberated, or via development of yellow colour.

It is therefore apparent that there are two possible methods of use :

(1) In the normal manner in acid solution, and protected from light.

(2) In alkaline solution as a powerful self destroying bactericide—in this manner it can usefully supplement the activity of more restricted, but more stable, preservatives.

The stability of *Bronopol* at 0.05% concentration in the two shampoo bases was followed, as in the PMN tests, by microbiological agar diffusion assay using *B. pumilus* or *E.coli* as test organisms.

The results are shown in *Table V* as percentages of the activity of solutions at pH 5.5 stored at 0–4°C, which appear to be stable.

Table V

Bronopol assays

Results of storage of *ESB3* and *TLP* dilutions in glass, in the dark, with 0.05% *Bronopol* in terms of percent activity remaining after specified storage period.

	pH 5.5				pH 8.0			
Storage period	0–4 °C	30°	45°	60°	4°	30°	45°	60°
30% *ESB*								
1 hour	100				100			
1 day	100	97	95	82	99	102	98	82
1 week	100	91, 97*	84, 83*	65, 40*	102	93	84	55
4 weeks	100	92, 98*	64, 46*	(<40)	102	98	54	(<40)
8 weeks	100	91	(<40)	(<40)	107	98	(<40)	(<40)
40% *TLP*								
1 hour	100				85			
1 day	100	99	94	60	98	53	(<40)	(<40)
1 week	100	78, 89*	65, 50*	(<40)	88	(<40)	(<40)	(<40)
4 weeks	100	85, 72*	(<40)	(<40)	(44)	(<40)	(<40)	(<40)
8 weeks	100	57	(<40)	(<40)	(<40)	(<40)	(<40)	(<40)

*Results from a separate experiment in which storage in polythene was compared with storage in glass.

(<40)—Result affected by shampoo base activity below about 40%.

It will be seen that the activity of *Bronopol* was maintained for 8 weeks at 30°C at both pH, in the presence of ether sulphate. In *TLP* solution, on the other hand, it was much less stable especially at pH 8.0.

Storage in polythene as opposed to glass showed little effect on the stability.

The fact that nonionic surface active matter has little or no effect on the antibacterial activity of *Bronopol* (11) was confirmed by lethal tests against strains of *Ps.aeruginosa* (*pyocyanea*) and *E.coli* using 0.1% *Bronopol*, with aqueous 4% solutions of *Tween 80, Myrj 52, Arlacel 83,* lecithin and cetomacrogol. All were lethal within 10 minutes.

In the presence of 30% *ESB3* and 40% *TLP*, this activity was maintained and concentrations of *Bronopol* as low as 0.025% were lethal within an hour at room temperature.

(*Received : 12th October 1964*)

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Introduction by Mr. Bryce

Principally, this paper is a collation of our company experience, and presents a point of view presumably not greatly different from that of any other technically competent organisation. Our thesis is that there is more to preservation than adding preservative. As an aspect of formulation, preservation cannot be dissociated from considerations of factory plant, process and pack.

In the case of a shampoo, it is necessary to bear in mind that straight chain alkyl and alkyl ether sulphates are among the most readily biodegradable of detergents. They are, in other words, susceptible to microbiological attack ; a situation that is recorded in the general literature references quoted, and by many published papers. Preservation amounts simply to ensuring that the finished shampoo is a sufficiently inimical environment to likely contaminant organisms to prevent their multiplication and, preferably, to kill them. In two respects, preservation of shampoos is easier

than the general run of cosmetic preservation problems. Firstly, shampoo ingredients, despite what has just been said, are antagonistic to a wide range of organisms. Secondly, contamination during use is not a serious factor in general, because of the nature of the packs used, the comparatively short period of use, and the improbability of consequential physical or chemical deterioration of the product. On the other hand, there is one respect in which it is vastly more difficult. Whereas small quantities of anionic surfactant generally potentiate the action of antiseptic and preservative substances, larger concentrations have a contrary effect by removing active material from the aqueous phase into the surfactant micelles. Few preservatives retain much activity under these conditions, which clearly gives rise to difficulty in practice.

We would emphasise that the figures quoted in respect of commercial shampoos are typical only of contaminated products. Many houses consistently maintain low or zero counts. The organisms found, being predominantly gram-negative bacteria, are likely to be derived mainly from water and raw materials, which may contribute in excess of 100,000 organisms/g. Our experience thus accords in general with the commonly accepted notion that anionic surfactants are active against gram-positive, but not against gram-negative organisms. We would, however, add that amine based alkyl sulphates, indeed alkyl sulphates in general, show some activity against gram-negative organisms provided that the concentration is sufficiently high. For example, 20% of triethanolamine lauryl sulphate might prove adequate for self preservation. Ether sulphates, on the other hand, appear to be almost devoid of activity against gram-negatives. The 28% solution as commonly supplied will certainly not prove lethal to them. We have also occasionally found heavy gram-positive contamination of material of this type.

In considering preservatives capable of satisfactory activity in shampoos, we find that phenyl mercuric salts are fully compatible with ether sulphates on the acid side of neutrality, and doubtfully so at pH 8. Formalin is much more generally applicable but has many disadvantages, especially marked reactivity with amines.

It was as a result of troublesome reactions between formalin and colouring matter that we first gave serious attention to *Bronopol*, one of a lengthy series of halogenated nitro aliphatics prepared in our research laboratories some years previously. Experimental formulation work commencing in 1959 had suggested that this compound might prove useful. This we have amply confirmed, finding particular application in the preservation of shampoos and nonionic stabilised emulsions. A tendency to break down above pH 7 with formation of formaldehyde suggests preferred use in acid solution, in which circumstances its activity is maximal. The decomposition mechanism suggested, I might add, is an "Aunt Sally" which can stand until somebody suggests a better. In any case it will probably vary with circumstances.

Light, as a deleterious agency, presents little difficulty in practice, but should certainly be borne in mind in connection with single phase systems in clear glass or polythene containers. Aqueous solutions of *Bronopol* are in fact colourless, and UV absorption only becomes significant below about 3500 Å. Optimum stability in water is believed to be attained at about pH 4.5 but use at higher pH is possible in practice. For example, a nonionic stabilised o/w emulsion at pH 5 showed no marked loss of activity after storage in a glass bottle in an artificial shop window for one year. This is a particularly severe test as this test location not infrequently attains temperatures in excess of 45°C in summer. Samples stored at 25°C showed no loss at all.

DISCUSSION

MISS D. L. SAMUEL : Are *o*phenylphenol and its esters, or tribromosalicylanilide of any value as preservatives in shampoos ?

MR. BRYCE : To be perfectly honest, in this connection we have not particularly looked at these materials. Possibly Mr. Smart may be willing to comment on tribromosalicylanilide. As far as *o*phenylphenol is concerned, we should regard it as unlikely to be suitable as a shampoo preservative. It may well have some activity but I do not think this is likely to be very great. I believe that Mr. Brodie has in fact experimented with *o*phenylphenol and would perhaps care to say a few words.

MR. F. SHAW : Mr. Brodie is not here, but I can confirm that he has tested this material and found it satisfactory in preserving the conventional type of shampoo on the market, namely, neutralized alkyl sulphates, a.s.o.

MR. R. SMART : We have not tried tribromosalicylanilide as a shampoo preservative, but would not expect it to be sufficiently active against the gram-negative bacterial species that cause trouble in shampoos.

DR. M. R. W. BROWN : I would like to suggest a preliminary method for screening antimicrobial agents, which permits an assessment of inactivation by such things as nonionic surfactants. The method may well save labour, time and cash. Replicate logarithmic phase cultures are grown in the appropriate medium, possibly containing inactivators, and graded concentrations of the chemical in question are added separately to the cultures. Alterations in the growth rate as observed spectrophotometrically give estimates of activity. With this method one worker can use about ten cultures in one day, and the results are immediately available.

DR. G. WHITEHOUSE : It is known that other chemicals which slowly break down with liberation of formaldehyde can be used as preservatives. In this context would you care to comment on the bactericidal properties of *Bronopol* in both alkaline and acid media ?

MR. BRYCE : Greater experts on that subject than myself are present at this meeting, but I would simply say that we have no evidence that *Bronopol* breaks down significantly to formaldehyde in distinctly acid medium. In my introductory notes I did in fact mention the practical stability of a product which, in general terms, might be regarded as somewhat unstable, provided that it is properly formulated in acid solution. I imagine that at least one of the hydroxyl groups present is significantly ionisable, and in alkaline solution, strictly speaking, we may not be dealing with the stability of *Bronopol* at all. In such circumstances we certainly tend to get formaldehyde and no doubt some of the microbiological activity is attributable to nascent formaldehyde. Nevertheless, observed activity is greatly in excess of that to be expected of a solution of formalin of corresponding strength. Of course, one of the difficulties in making comparisons of this sort is that formalin can be such variable stuff.

MRS. H. BUTLER : In view of your remarks on the difficulties of preserving shampoos, would you please comment on the current trend towards marketing medicated shampoos. If the raw materials need preserving and are liable to be heavily contaminated, how do we expect to back the theory behind medicated shampoos ?

MR. BRYCE : This is a very good point. I would suggest that if the medicament in a shampoo is not capable of preserving the product adequately due to the effect of the surface active matter, the only conditions under which it is likely to show antimicrobial activity on the scalp is when the preservative or medicament is removed from the shampoo system, and built up in the skin of the scalp. Otherwise I should be surprised to find much activity due to such medicament ; but, problems of this type require an experimental approach–not mere theorising.

J. Soc. Cosmetic Chemists **16** 203-220 (1965)

Measurement and Prevention of Oxidative Deterioration in Cosmetics and Pharmaceuticals

J. P. OSTENDORF*

Presented at the Symposium on "Preservatives and Antioxidants", organised by the Pharmaceutical Society of Great Britain and the Society of Cosmetic Chemists of Great Britain, in London on 17th November 1964.

Synopsis—Oxidation mechanism, and the factors that are responsible for the initiation of oxidation are reviewed. The various methods with which the oxidation can be traced are mentioned. With this knowledge in mind the prevention of oxidation is reviewed. First the mechanism, then the various general precautions to be taken, and the antioxidants. Examples are cited.

Introduction

If a cosmetic or pharmaceutical preparation undergoes any change during storage, such change will affect the usefulness of the preparation, because the action of any mixture is based on its composition at the time of, or immediately after, its manufacture. Changes which occur may be of different types. Firstly, purely physical ones, such as the drying or disintegration of emulsions ; secondly, and these occur frequently, changes caused by micro-organisms, and thirdly, purely chemical changes, namely oxidation.

Oxidation Phenomena

Theoretically all organic compounds can oxidize. Of course, some substances will be more sensitive than others. Among those substances which are especially inclined to oxidize are vitamin-preparations (especially

*N.V. Chemische Fabriek "Naarden," Bussum, Holland.

vitamins A,B,C,D,E, and K), essential oils and perfumes. Furthermore, practically all oils and fats are apt to oxidize. From among the pharmaceuticals we can mention adrenalin and penicillin. Many plastics, rubber, petrol, etc., also deteriorate as a result of oxidation. The oxidation process can reveal itself in many ways, such as changes in smell and flavour, or discoloration and brittleness as in the case of plastics. Oxidized oils can become toxic, and irritate the skin.

The Concept of Oxidation

By oxidation we mean autoxidation, i.e. the reaction of a chemical compound with oxygen without drastic external interference.

In autoxidation we are confronted with a chain reaction, in which we can discern three different steps, namely initiation, propagation and termination.

Mechanism of Autoxidation

Initiation

$$\text{initiator} \longrightarrow \text{free radicals } R^{\bullet}$$

Propagation

$$R^{\bullet} + O_2 \longrightarrow RO_2^{\bullet} \quad \text{(peroxy radical)}$$
$$RO_2^{\bullet} + RH \longrightarrow ROOH + R^{\bullet}$$

Termination

$$\left.\begin{array}{l} RO_2^{\bullet} + RO_2^{\bullet} \longrightarrow \\ RO_2^{\bullet} + R^{\bullet} \longrightarrow \\ R^{\bullet} + R^{\bullet} \longrightarrow \end{array}\right\} \text{inactive products}$$

A normal organic compound, the initiator, is in some way or another changed into an active particle which is called a radical.

For this reaction a fairly large amount of energy is required, as can be produced, for instance, by light, especially ultra-violet light, and by heat.

Furthermore it is also possible that labile organic compounds such as peroxides easily split into free radicals. Metals, like copper and iron, can also promote the formation of these radicals.

The most important initiators of the chain reaction are therefore

light,
heat,
peroxides or other labile compounds,
heavy metals like Cu and Fe.

Propagation is the actual chain reaction. Here the free radical $R^{\bullet}$ can

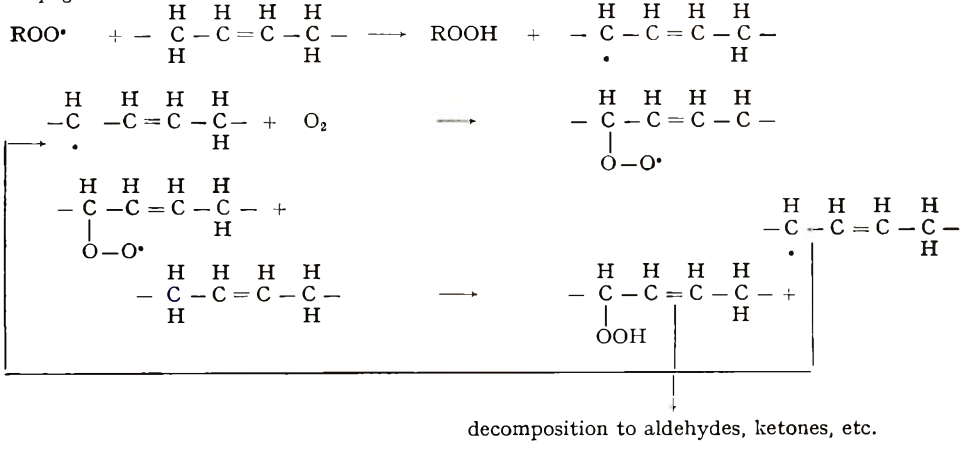
take up one mol of oxygen to form the new radical $RO\cdot_2$, named a peroxi-radical. The latter can react with a molecule of *RH* to form a peroxide *ROOH* plus a new radical $R\cdot$, which once more is able to take up a molecule of oxygen, etc., etc. Theoretically this chain reaction can continue until either all of the oxygen or every molecule of *RH* has been used up.

But that does not happen quite so easily, because the radicals can react with one another. This is called the *Termination* step, because it breaks the chain. If two radicals meet each other the process is broken off. This is illustrated by the autoxidation of unsaturated fatty acids.

Autoxidation of unsaturated fatty acids

Initiation

Propagation



decomposition to aldehydes, ketones, etc.

In the case of an unsaturated fatty acid the *H* atom near the double bond, the so-called allyl hydrogen atom will be the least firmly bound. Here oxidation will catch a hold as illustrated.

The final product of this oxidation will be a peroxide.

By themselves these peroxides are flavourless and odourless, and will not give rise to any off-flavours. A peroxide function next to a double bond is, however, labile, and there are many ways in which they can decompose into compounds which have the typical odour of rancid fats.

Measuring Oxidation

In the course of time many methods have been developed for measuring the degree of oxidation. There is the peroxide determination of Wheeler. A number of minor alterations have been made to it, but the principle

has remained unchanged. This method is based on the property of peroxides to release iodine from potassium iodide in an acid medium. The iodine which is liberated can be titrated with sodium thiosulphate.

$$ROOH + 2HI \longrightarrow I_2 + ROH + H_2O.$$
$$I_2 + 2Na_2S_2O_3 \longrightarrow Na_2S_4O_6 + 2NaI$$

The amount of "thio" needed is thus an indication of the amount of peroxide present. This quantity is expressed in milli-equivalents peroxide/kg fat, and is called the peroxide value (P.V.). In England the Lea value is sometimes used, being exactly double the peroxide value.

This method is hampered by one complication, namely that the presence of water disturbs the reaction. But if we take care that the total amount of water in the sample does not exceed 3 ml the results will be reliable.

In the case of complicated preparations it is advisable to extract the fat or fat solubles which are the parts most prone to oxidation, by means of chloroform under carbonic acid to exclude the oxygen.

Another test which is often used is that known as the *TBA test.* TBA stands for thiobarbituric acid. In contrast to determining the peroxide value, this test is based on the determination of malondialdehyde. This substance is produced from strongly unsaturated compounds by breaking down the peroxides which are formed.

The test consists of heating the sample together with thiobarbituric acid in the presence of a strong acid. If malondialdehyde is present a red colour appears which can be measured spectrophotometrically.

Another test is the *Kreis test,* which is based on the formation of epihydrinaldehyde derivatives as secondary products. The method consists of dissolving approximately 3 g of fat in benzene. The solution is shaken well with conc HCl for 1 min, and then a few drops of phloroglucinol dissolved in alcohol are added.

The intensity of the red colour which appears after shaking is some indication of the degree of oxidation which has taken place in the fat. For more complex products this test cannot be used, because the result is sometimes influenced by the presence of other substances.

It goes without saying that vitamin preparations, and similar products should preferably be tested on their vitamin content.

Determination of Storage Qualities

The research chemist, and the manufacturer of toilet preparations, are always anxious to predict the storage qualities of their products. The

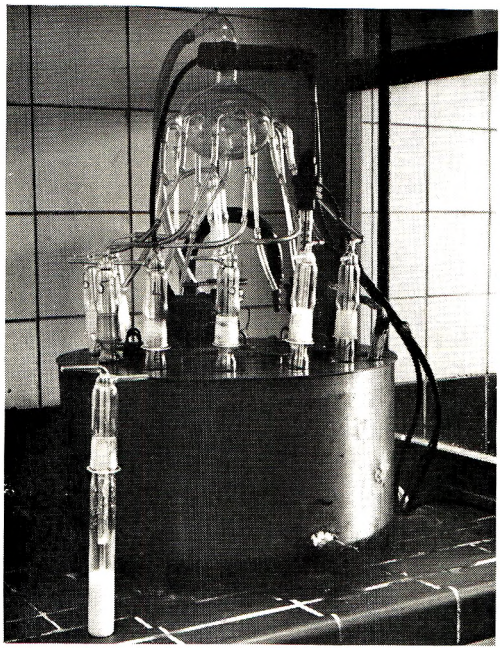


Figure 1

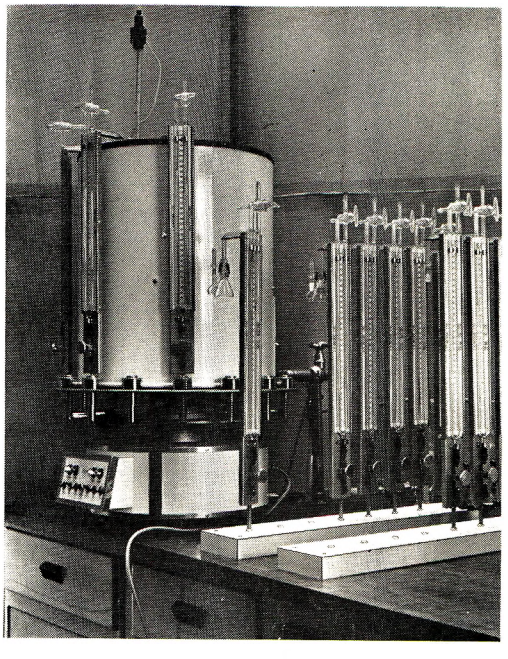


Figure 3

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soundest method of doing this is to make a series of tests as above, at different times, thereby following the degree of oxidation in the product. This calls for patience on everyone's part.

Much work has been carried out in order to find a method by which the oxidation process could be accelerated. Several different methods were indeed developed, but each of them has its limitations, and for each one the correlation with the actual storage properties has to be determined separately.

The method generally used in fat chemistry is the one known as the *Swift Stability Test*, or the *Active Oxygen Method*.

This involves passing dried air or oxygen at a controlled rate through samples of fat maintained at a temperature of approx. 100°C until the samples become rancid.

Figure 1 illustrates the apparatus used for this method.

The peroxide value of the sample is determined periodically, and the values obtained are plotted against time (*Fig. 2*).

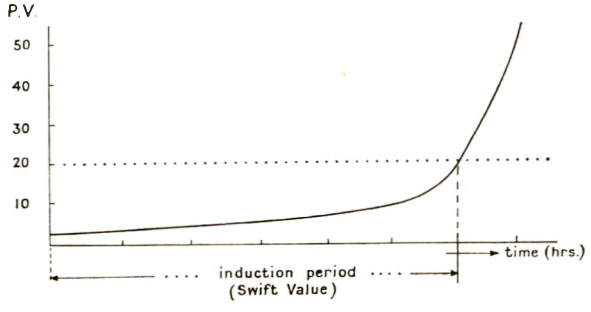


Figure 2

It was noticed that oxidation took place more rapidly after a definite time. The initial period, which is usually taken to be that up to the point where a peroxide value of 20 has been reached, is called the induction period. The Swift Value is defined as the time needed to reach a *P.V.* of 20 under AOM conditions. Sometimes, another limit is taken, e.g. *P.V.* 50 or 100. A similar curve will be found in most cases when we take periodical peroxide value measurements of a product in actual storage.

Apart from this method, extensive use is also made of the oxygen absorption methods. For this purpose, the so-called Warburg-Barcroft apparatus (*Fig. 3*) is used, which was originally developed to measure metabolism of biological material, but which proved to be extremely useful

for the measurement of oxidation rates. The degree of oxidation in a preparation is measured by determining the quantity of oxygen absorbed over a definite period. The apparatus consists of a basin which is kept at a constant temperature of 30° or 40°C. A number of small flasks, each of them connected to a manometer are suspended in this bath (*Fig. 4*).

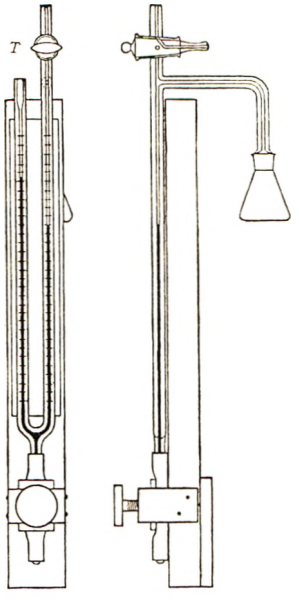


Figure 4

The flasks are shaken in order to ensure that the oxidation rate is not limited by the diffusion rate of the oxygen through the sample. By taking readings from the manometer the amount of oxygen used can be determined to the nearest cmm. The advantage of this method is that the course of the oxidation-reaction is no longer of importance. It is immaterial whether peroxides or aldehydes are formed, because the overall amount of oxygen is measured. It is equally unimportant whether the samples are volatile, as a closed system is being used. It is a further advantage that the amount of material tested can be very small, even $\frac{1}{2}$ g is sufficient. Even very expensive products can therefore be tested in this way. On the other hand, this method will not yield results as quickly as the Swift apparatus.

Another method, also based on the uptake of oxygen is the *Oxygen Bomb Test*, frequently used in the petrochemical industry to measure the

stability of lubricating oils. The sample is filled into a steel bomb and is put under oxygen pressure of up to 100 psi. The end of the induction period is marked by a sudden pressure drop. Other variations on this principle have been suggested, and some of them are actually used.

The so-called accelerated storage test is another method which is used quite frequently. The sample, preferably with a large surface exposed, is stored in a laboratory stove or humidity cabinet, and is tested periodically to determine the degree of oxidation. The speed of the reaction will depend on the exposed surface and on the temperature, which can be chosen at will without changing the physical properties of the preparation. This method is also frequently used, because although not rapid, it is fairly simple. An ageing process which is 3 to 5 times as fast as that under normal storage conditions can be obtained.

Prevention of Oxidation

General precautions to be taken

(1) Exclusion of *light* — dark coloured flasks,
— U.V. absorbers in transparent wrappings.

(2) Avoid *high temperatures* — cool storage.

(3) Avoid *peroxides* — use fresh materials,
— control raw materials.

(4) Avoid *heavy metals* — use stainless steel or glass apparatus,
— use sequestering agents (citric acid, EDTA).

(5) Minimize the *surface*

(6) *Antioxidants*

Light can be excluded by choosing a packaging material impermeable to light. From a commercial viewpoint that might not always be attractive, as one likes to display the content. If transparent plastic foil is chosen it is recommended that the ultra violet rays should be absorbed by having a UV absorber processed into the plastic. These absorbers are closely related to the substances which are applied in suntan preparations, e.g. benzophenone derivatives or benzotriazoles.

The influence of *heat* can be eliminated by keeping the temperature of the product as low as possible during storage.

The influence of *peroxides* can be counteracted by using fresh oils and fats. Scrupulous quality control of these raw materials is advisable, including a check of the peroxide value. At the beginning the *PV* should preferably be zero, but in practice a *PV* of 2 for animal fats, and about

5 for vegetable oils can be tolerated. As regards the *metals* which promote oxidation, copper and iron have been mentioned, but other metals, such as cobalt, manganese, tin, etc., also stimulate oxidation, although to a far lesser degree.

As far as possible iron and copper apparatus should be avoided during manufacture of products, and in the handling of raw materials which are susceptible to oxidation.

From my own experience I know that 0.05 ppm of copper will cause a considerable acceleration of the oxidation velocity of fats. Iron is approximately ten times less active, which means that a minimum of 0.5 ppm of iron will be able to accelerate the rate of oxidation. Experience has proven that stainless steel is by far the best to use. In the case of exceptionally sensitive preparations it will probably be better not to use any metal at all, but rather glass or glass-lined metal.

To render the traces of metal, which will unavoidably be present, inactive so-called sequestering agents are frequently used. With foodstuffs, citric acid is most commonly used, while one of the most active ones is EDTA. In the U.S.A., this product is already being allowed in certain foodstuffs, although only reluctantly. It is difficult to predict whether other countries will follow suit.

For cosmetics and other non-edible preparations, the addition of EDTA is most advisable, especially in soaps.

Another important factor is the surface area of the product which comes into contact with air. The larger this area, the quicker the oxidation ; and the oxidation will continue until all the available oxygen has been consumed. The oxygen available at the surface is unlimited unless the packing seals it off. Within the preparation the oxygen has to be supplied by diffusion, which is a slow process. In airtight bottles it is possible to remove all the oxygen by means of additives such as ascorbic acid, or an enzyme combination which oxidizes glucose to gluconic acid. Plastic packing materials, especially polyethylene is permeable to oxygen, so that products packed in this material should not be considered sealed off from the air. This point should be considered when choosing packing materials.

Antioxidants

Antioxidants are substances which, when added in small quantities, retard or delay oxidation. They do not provide total prevention.

Propagation step:

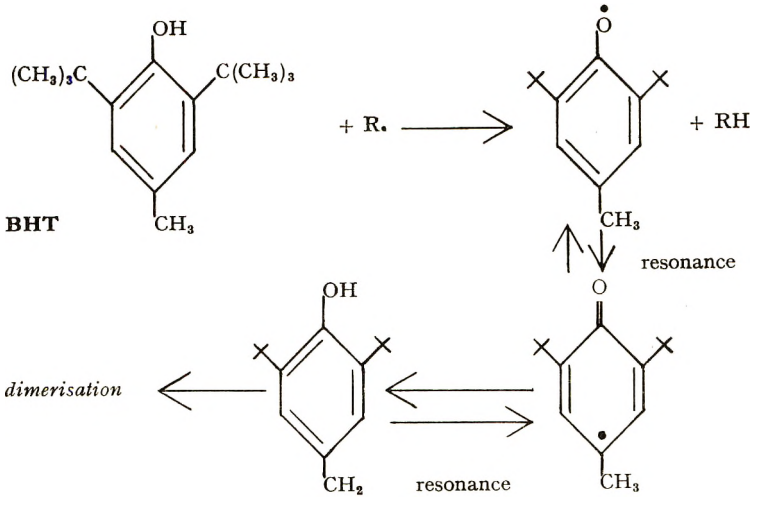
$$R^{\bullet} + O_2 \longrightarrow RO_2^{\bullet}$$
$$RO_2^{\bullet} + RH \longrightarrow ROOH + R^{\bullet}$$

$$R^{\bullet} + AH \longrightarrow RH + A^{\bullet}$$
$$RO_2^{\bullet} + AH \longrightarrow ROOH + A^{\bullet}$$

$$A^{\bullet} + RH$$
$$A^{\bullet} + A^{\bullet} \longrightarrow A - A$$
$$A^{\bullet} + R^{\bullet} \longrightarrow AR$$

To keep the chain reaction going, a reactive radical $R\cdot$ or $RO\cdot_2$ is needed. The antioxidant *AH* has the property to react with these radicals, thereby forming the radical A, which is not sufficiently reactive to sustain the chain reaction. The antioxidant radical is sometimes able to react with itself, thus forming the dimer *AA*.

Sometimes such a radical can also form a stable compound in another way, for instance by reacting with a radical $R\cdot$, as illustrated in the following diagram.



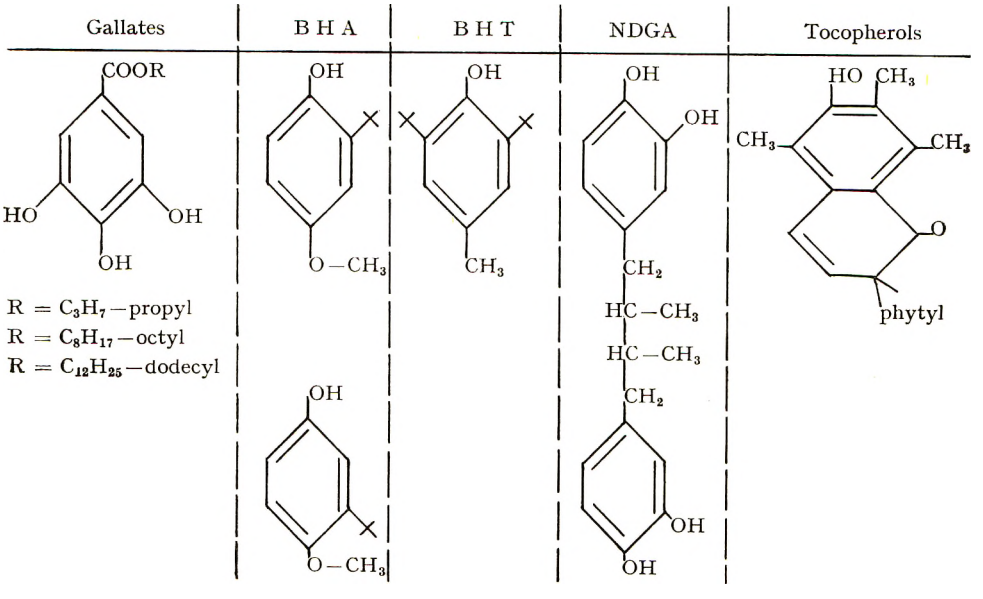
BHT is a phenolic antioxidant. The tertiary butyl groups in the ortho position are so bulky that the phenolic *OH* group is completely shielded. The phenoxy-radical which is formed can stabilize itself by resonance, and in certain circumstances it can dimerise.

It is therefore clear that the antioxidants themselves are used up—they are oxidized. Because of this an antioxidant can never protect a fat against oxidation once and for all.

It now becomes clear why the addition of an antioxidant will have little or no effect when a substance has already been partially oxidized, i.e. when the chain reaction is in full swing and many free radicals have been formed. All antioxidant molecules will immediately be destroyed, and an antioxidant must therefore be added at the earliest possible stage.

It is possible to compare autoxidation with the starting of an aircraft. Initiation corresponds with the starting up of the engines. For this, electric energy—in our case light—is needed. Then follows propagation, i.e. the aircraft taxies along. Speed increases, oxidation gains pace, until the aircraft takes off—which is at the end of the induction period; the oxidation curve as shown by the Swift test apparatus, shows an upward curve. The function of our antioxidant can be compared to the brakes on the aircraft wheels. The start will be retarded. The aircraft will need a longer run to gather enough speed for the take-off. In other words the induction period is prolonged. Once the aircraft is airborne a brake on its wheels is perfectly useless. Similarly, as soon as oxidation has advanced to a certain stage, the addition of an antioxidant serves no purpose at all.

The most frequently antioxidants are



Gallates (*Gallic acid esters*)

The most commonly used esters are the propyl, octyl and dodecyl esters. The latter two are easily soluble in fats. Propyl ester is more soluble in water than in fats.

These are sound, effective antioxidants, often used in the food industry. It is a disadvantage that they discolour in the presence of iron and its salts. In most cases this can be prevented by adding a sequestering agent. Octyl and dodecyl esters are heat-resistant and non-volatile with steam. These antioxidants can be used in bakery goods, and frying oils. This we call the carry-through property.

Butylated hydroxy anisole (*B.H.A.*)

Chemically this antioxidant is a mixture of two isomers. It is very effective, heat resistant and hardly volatile with steam. This is also widely used in the foodstuffs industry.

Butylated hydroxy toluene (*B.H.T.*)

An antioxidant developed by the petrochemical industry for its own use. At the moment there is a furious discussion about its toxicity in food. In some countries its use in foodstuffs and medicaments has been prohibited.

It is a good antioxidant, but it has poor carry-through properties.

Nordihydro guaiaretic acid (*N.D.G.A.*)

This is a slightly older antioxidant, which is extracted from a desert plant. It is very effective, but even in small dosages it has a slightly bitter taste. The American Army used it in its fat supplies during the Second World War. When so many less expensive synthetic antioxidants appeared on the market after the war, this compound lost its pre-eminence.

Tocopherols or vitamin E

These natural substances are themselves rather prone to oxidation and therefore not quite as suitable as the synthetic ones. Yet they are widely used, as a result of the urge to produce purely natural foodstuffs. The smell of oxidized tocopherols is slightly reminiscent of fish, which can be a disadvantage in some foods. Most vegetable oils in their natural state contain considerable amounts, e.g. 0.1–0.01%. Animal fats also contain tocopherols, but to a far lesser degree.

Mixtures

It is sometimes advantageous to choose a mixture of antioxidants, and achieve synergism. Occasionally, if mixtures are used, the same result can

be obtained with only $\frac{1}{3}$ of the total amount of additive. A mock synergism occurs when we add a sequestering agent to the antioxidant.

The most effective procedure is the use of a balanced antioxidant mixture, consisting of at least two antioxidants and a sequestering agent, and many such mixtures are on the market. To facilitate handling, the ingredients are dissolved in a solvent, e.g. an inoffensive glycol or a suitable oil.

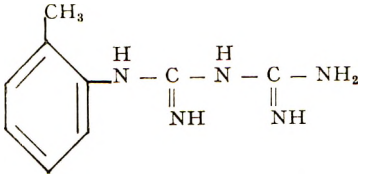
When using antioxidants in emulsions, it is necessary to ensure that they are preferentially soluble in the phase where the substances most prone to oxidation are situated. In general this will be the fat phase. Most antioxidants comply in this respect, except propyl gallate which is more attracted to the water phase.

pH

All the antioxidants mentioned are phenols, and if the water phase has a pH above 7, there exists the possibility that they may be extracted by the water in the form of salts. Experience has shown that antioxidants lose their effect at a higher pH, and the risk of discoloration is increased.

Apart from the phenolic antioxidants there are a large number of aminic antioxidants, i.e. substances having an amino group, which are widely applied in technical materials such as rubber and plastics. This type of antioxidant is not used in foodstuffs on account of toxicity, and it often causes discoloration as well.

The one exception is *o*toluyl biguanide.



This substance is an excellent antioxidant for soaps, if necessary in combination with EDTA.

In most countries all the antioxidants mentioned, except *o*toluyl-biguanide are permitted for use in foodstuffs. They have been tested extensively in respect of their toxicity, and found to be harmless in the prescribed dosages.

Antioxidants for skin preparations must meet another specification, namely they should not be irritating to the skin. We found that some

gallates should be avoided in such preparations because they may irritate the skin of certain individuals, perhaps because they are sensitized by gallates in foodstuffs.

Action of Antioxidants and Sequestering Agents

As a first example refined lard has been chosen as a substrate. This fat is often used for testing purposes because it oxidizes quickly and reacts favourably to the addition of antioxidants, in contrast to many vegetable oils.

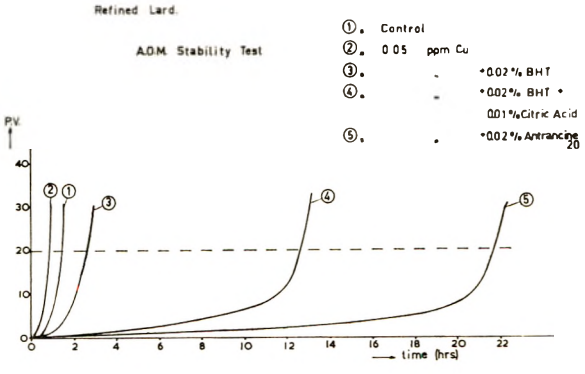


Figure 5

Figure 5 shows the result of a Swift stability test carried out at 100°C. The curves were obtained by determining the peroxide value periodically.

Curve 1 is the control, i.e. without additives. Swift value approx. $1\frac{1}{2}$ hr.

Curve 2 was obtained after adding 0·05 ppm Cu in the form of Cu oleate. We clearly see the pro-oxidative action. The Swift value dropped to $\frac{3}{4}$ hr.

To this fat, contamined by Cu, we added BHT, and curve 3 shows some antioxidative effect, but the result is poor. If citric acid is used as a sequestering agent in combination with BHT a considerable improvement is brought about (curve 4). Using a "tailor-made" antioxidant mixture consisting of octyl gallate, BHT, BHA and citric acid, an even better result is obtained with the same overall dose despite the fact that 70% of the antioxidant mixture consists of an inactive solvent.

The second example concerns lanolin.

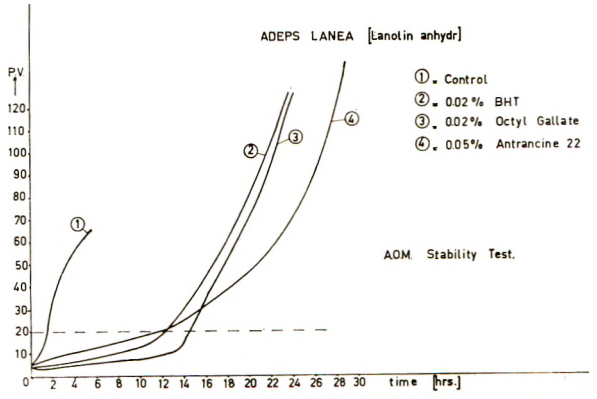


Figure 6

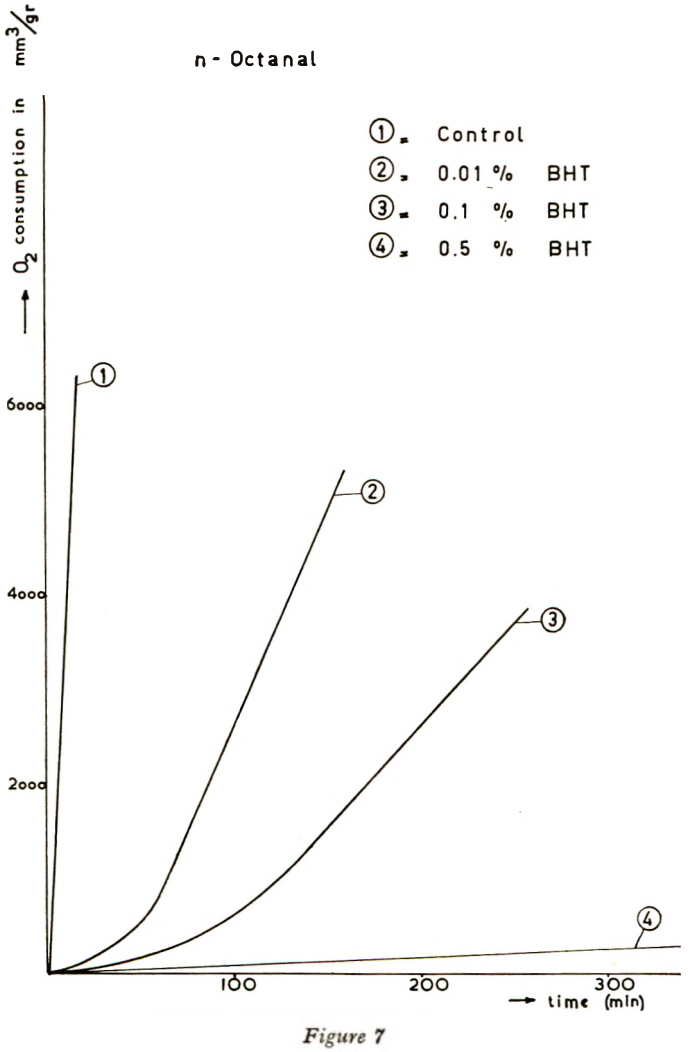


Figure 7

In *Fig. 6* we notice that it becomes more difficult to interpret the data. The curves intercept each other. The lower *PVs* seem to indicate that octyl gallate should be used, while the higher *PVs* apparently call for BHT which initially seemed less effective.

Each quality of lanolin reacts differently. Sometimes the iron content is considerable. It is advisable to draw up a similar diagram for each type of lanolin, and to choose the most effective antioxidant with the help of that.

Stabilization of aldehydes represents the third example.

These substances, such as *n*octanal, are so volatile that they cannot be tested with the Swift apparatus. For their treatment, the Warburg apparatus can be used to good effect.

In *Fig. 7*, curve 1 is again the control, while the curves numbered 2, 3, and 4 were obtained by adding ever increasing dosages of BHT to the aldehyde. A distinct decrease in the amount of oxygen consumed is noted. The temperature was kept constant at 40°C, and the size of the sample was 0.5 g. In this instance the Warburg apparatus enabled us to obtain a quick indication of the effectiveness of the antioxidants.

(*Received : 9th September 1964*)

Introduction by the lecturer

I will quote one example of the influence of some minor constituents on the stability of a fat. A confectioner, making certain sweets containing fat, was not satisfied with the shelf life of his product, because it turned rancid in a few weeks.

We investigated the fat phase. *Fig. 8* shows the result of a Swift stability test carried out at 100°C. The fat used is the control, viz. a hydrogenated palm oil. The stability turned out to be 70 Swift hr which is quite satisfactory. The flavour composition used had a vegetable oil as solvent, so we first tested the influence of this oil. It is remarkable that the oil acts as an antioxidant, increasing the stability to about 110 hr. The next step was the addition of the flavour to this mixture. The stability again decreased to about 70 hr. This addition too could not explain the bad shelf-life. We then investigated the copper content of the entire product and found it to be about 2 ppm. We also added this amount of copper to the fat, Swift tested and found that the stability of the composition decreased to about 10 hr, thus indicating the reason for the effects experienced.

DISCUSSION

MR. D. HELLIER : In discussions of antioxidant activity such as this, the emphasis is always laid on the addition of relatively pure, synthetic chemical substances as antioxidants. We wish to draw attention to the fact that ingredients which are often used for other purposes in the formulation of food and cosmetic preparations may also have useful antioxidant properties.

The existence of marked antioxidant activity in oatmeal, and extracts of oats, was

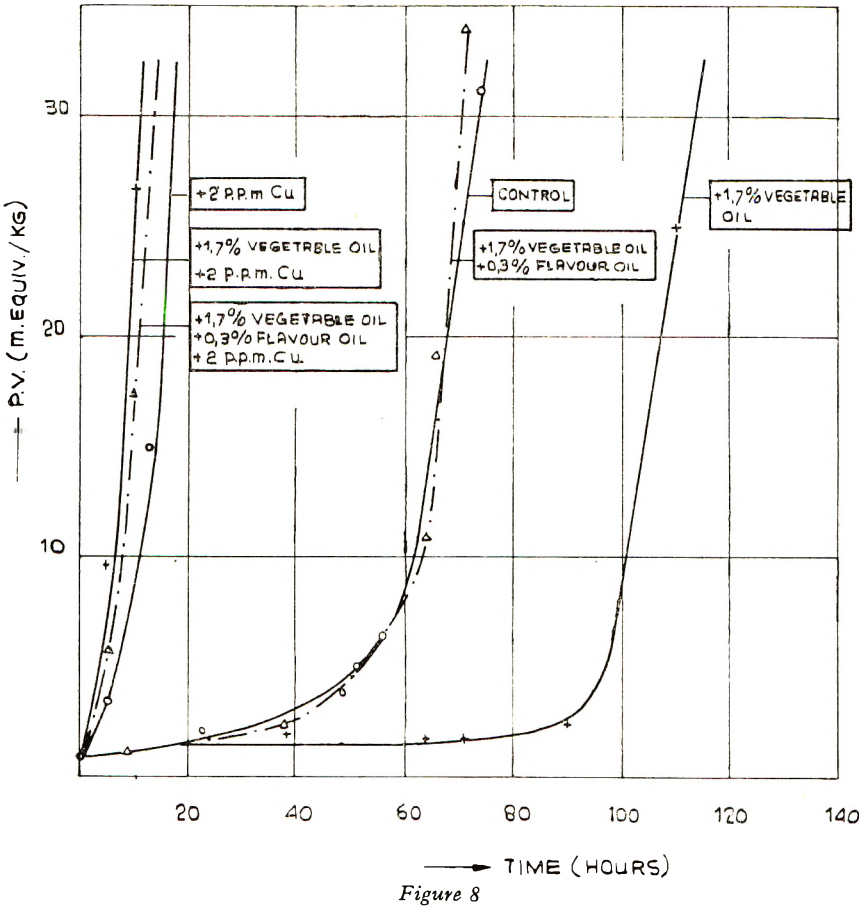


Figure 8

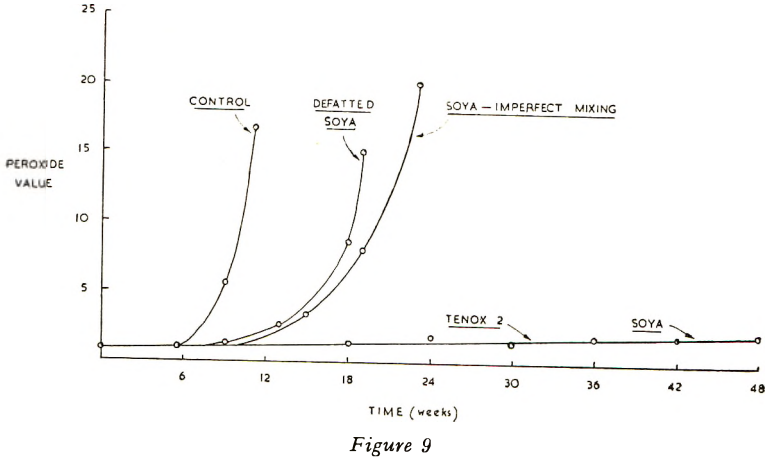


Figure 9

reported over thirty years ago and slightly later soya was reported by Lampitt and others as having a useful antioxidant activity. More recently we have re-examined these findings and have demonstrated that soya has a pronounced antioxidant activity with effective carry-over in baked products. These results were reported at the first International Congress of Food Science and Technology two years ago, but unfortunately the Proceedings of that congress have not yet been published.

We would now like to present some more recent results in which the effectiveness of soya as an antioxidant has been compared with that of a chemical antioxidant blend. *Fig. 9* shows the change in peroxide value with time, of the control formulation without antioxidant, of a formulation in which a defatted soya was blended with the fat, and one in which our own brand of full-fat soya was contained in the formulation but had not been blended with the fat first, and of two others in which the fat was blended with either our own brand of soya or with the chemical antioxidant. It is quite clear that the fat in both these last two samples was very effectively protected against oxidation for over a year although the conditions of storage, 20°–25°C in tins with loosely fitting lids, were adverse. The middle curve, imperfect mixing, shows how important it is from this point of view to ensure that the fat is adequately blended with the soya in order to achieve adequate protection.

In these experiments the fat used was lard and the three samples whose peroxide values rose in the sharp fashion indicated by the first three curves were quite definitely organoleptically rancid when the experiments were stopped. The other two samples which had shown very little change in peroxide value over 52 weeks showed no sign of organoleptic rancidity at the end of that time. In our laboratories, results of a similar general character have been obtained, with vegetable fat as well as with lard.

THE LECTURER: You stated that it is better to use naturally occurring antioxidants if they have the same effect as synthetic ones. I mentioned in the paper the use of the tocopherols as antioxidants. These products occur naturally in most vegetable oils, and are actually isolated from these oils as tocopherol concentrates, which are used as antioxidants. Nowadays, however, they are also made synthetically. In our laboratory we found that the 50% concentrates can be more effective than the pure synthetic ones, probably because they contain some other products that have a synergistic effect with the tocopherols.

The gallic acid esters are only partially synthetic products. Gallic acid itself is a pure natural product and a quite normal constituent of the tannins of tea and many other foodstuffs. The two antioxidants, BHT and BHA, are completely synthetic.

Many extracts from vegetable products have some antioxidant effect. We ourselves investigated the extracts of cocoa shells and found that they had a good antioxidant effect. In Israel, Dr. Zimmermann isolated antioxidants from orange peel. In the U.S.A., Gossipol was isolated from cotton seed oil, and this substance proved to be a very effective antioxidant, but it also proved to be highly toxic!

We conclude that antioxidants frequently occur in nature, but they must be screened toxicologically just as the synthetic ones.

On the effect of mixing your soya product with lard, I should like to state that the difference in effectiveness when using different procedures indicates that the antioxidant in the product is not so fat-soluble, which is a disadvantage for a good antioxidant. The antioxidants should dissolve completely in the fat phase.

MR. N. J. VAN ABBE: Do you regard *o*toluyl biguanide as having a low toxicity,

and being comparatively free from discoloration? Apart from its use in soaps, has it any other possibilities, e.g. what is its useful pH range for antioxidant efficacy?

THE LECTURER : *o*Toluyl biguanide is only used in soaps. In oils and fats it gives some discoloration, although it is an effective antioxidant in this substrate.

Due to its basic character, *o*toluyl biguanide reacts with acids like oleic acid, stearic acid and other fatty acids. This antioxidant should also only be used in products with a pH > 7. Little is known about its toxicity, and it is not permitted in foods.

MR. D. M. BRYCE : Have you any knowledge or experience of the possible utility of dilaurylthiodipropionate, or other peroxide scavenger, in cosmetic formulations ?

THE LECTURER : The esters of thiodipropionic acid, like the lauryl ester, are widely used in plastics, such as polyethylene and polypropylene, as synergists next to phenolic antioxidants like BHT. In the U.S.A. their use in foods is permitted. We once tested the lauryl ester in our laboratories, but it proved to be a poor synergist to antioxidants in lard. Citric acid was a better synergist in this case.

PROF. DR. F. NEUWALD : What do you think of ascorbic fatty esters as antioxidants, especially for foods? Their use is permitted in Germany.

THE LECTURER : The esterification of ascorbic acid leads to a better fat-soluble product. The solubility in fats of the palmitic ester, however, is still low. It is not quite 1% and it is therefore impossible to make antioxidant mixtures with a fatty oil as a solvent using this product.

I agree that the partition coefficient is greater for the ascorbyl palmitate than for the ascorbic acid itself, making it also more useful in emulsions. However, due to its price, the use of this ester is restricted.

MR. J. F. SMITH : Do you have any evidence for the partitioning into the aqueous phase of a two-phase system of antioxidant under the conditions of the Swift test?

THE LECTURER : An emulsion cannot be investigated with the Swift test. The temperature is too high, so the water would evaporate. One has to use an accelerated storage test, or the oxygen bomb test for investigating the oxidative behaviour of emulsions. Most antioxidants mentioned are completely lipid-soluble, and hardly or not at all water-soluble. Propyl gallate is the most water-soluble antioxidant of the materials mentioned.

MR. J. T. REES : In page 210 you refer to the use of an enzyme combination in removing oxygen from airtight packs. Would you please elaborate on this, and state whether it is desirable to include the enzymes with or apart from the product?

THE LECTURER : It is indeed possible to remove the oxygen from a container by using a sachet containing the enzyme combination, and a glucose solution. This sachet can be used, for example, in tins of milk powder or other dry products.

If, however, the preparation contains water, the enzyme system had better be incorporated in the product, in order to obtain a better effect.

J. Soc. Cosmetic Chemists **16** 221-236 (1965)

Protection of the Pack and its Contents against UV Light

A. R. BROWN*

Presented at the Symposium on "Preservatives and Antioxidants", organised by the Pharmaceutical Society of Great Britain and the Society of Cosmetic Chemists of Great Britain, in London on 17th November 1964.

Synopsis—The life and value of plastics packaging materials are increased by incorporating additives which protect them from the damaging effects of the ultra violet radiation present in natural and artificial light. The theoretical background is given with a review of the commercial ultra violet absorbers available for plastics use in the packaging of cosmetics.

Plastics materials are widely used for packaging as they are robust, yet light and resistant to chemical and solvent action. When left standing in daylight for long periods, they suffer the disadvantage that deleterious changes occur, often of sufficient severity to be seen by the eye. *Table I* shows the effects of sunlight on some commonly used plastics.

Table I

Cellulose	Weakens
Cellulose acetate	Weakens
Cellulose nitrate	Yellows and cracks
Epoxy resin	Darkens
Polyamide	Weakens
Polyester	Yellows
Polyethylene	Discolours
Polyformaldehyde	Chalks
Polypropylene	Cracks and crumbles
Polystyrene	Yellows
Polyvinyl chloride	Blackens

Some of these effects are due to oxidation which may be initiated by ultra-violet light, or by heat. Oxidation can be reduced to acceptable levels

*General Chemicals Division, Cyanamid of Great Britain Ltd., London, W.C.2.

by the use of antioxidants. These function, by chemical reaction, at reactive sites on polymer chains susceptible to oxidation, by preferential reaction with atmospheric oxygen or ozone or it is believed, in some cases, by sequestering catalytic ions.

Ultraviolet degradation, on the other hand, is countered by physical means, i.e. by cutting off the ultraviolet radiation from the plastics materials. Sunlight as received at the earth's surface consists of three radiation levels: 45% is infra-red—the long wave heating end of the spectrum; visible light accounts for 50% of the energy, and the remainder is ultraviolet radiation, 5% of the total, with a wavelength shorter than 4000 Å (400 mμ), as shown in *Fig. 1*. Although the ultraviolet light

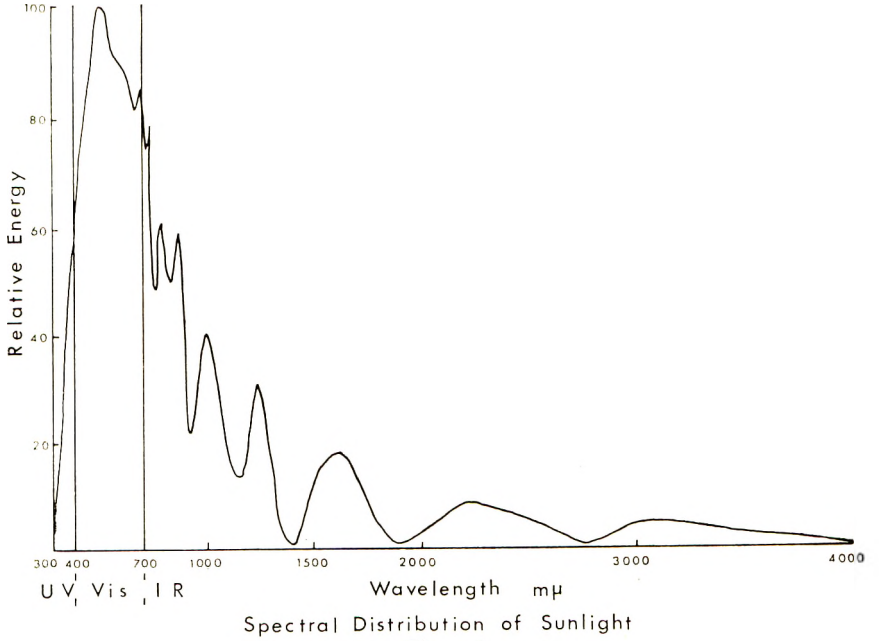
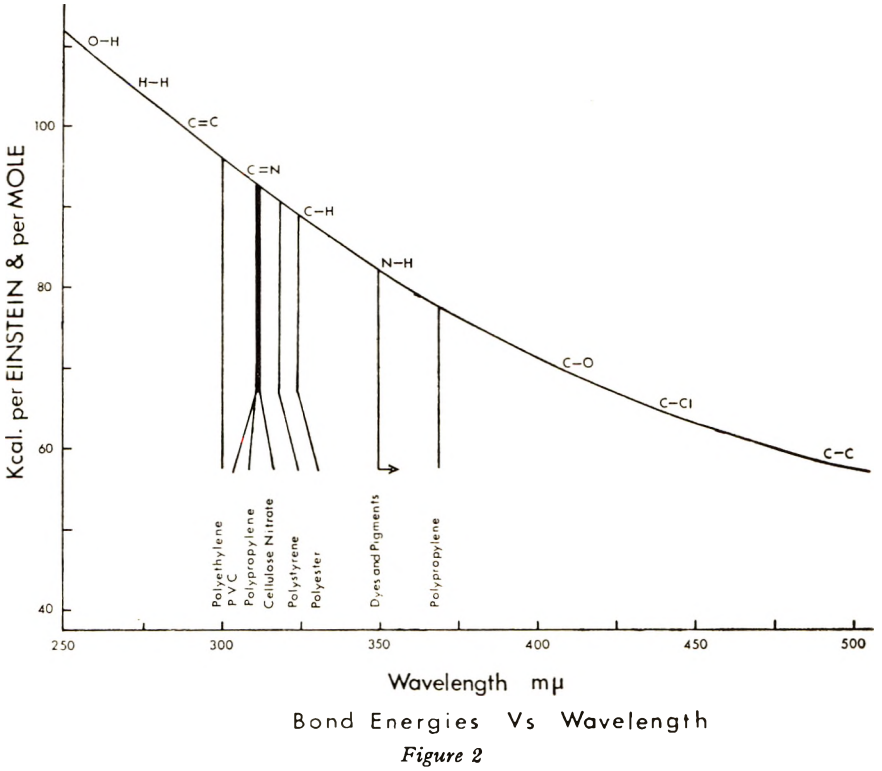


Figure 1

fraction is small, it is responsible for most of the damage to plastics, fabrics, dyes, pigments and even to the colour of wood, since the energy content of radiation is inversely related to the wavelength. Within the ultraviolet region the energy levels are sufficiently high to initiate chemical reactions—for instance the scission of bonds. Some of these levels are shown in *Fig. 2*, with the critical wavelength of light for a variety of plastics superimposed. The spectrum of fluorescent lighting tubes extends into the

ultraviolet region so the environment for any plastic material is therefore unfavourable, and protection against ultraviolet light is essential for a long and stable life.



Bond Energies Vs Wavelength

Figure 2

Either an external screen or incorporation of a UV absorbing substance is possible. The former is often awkward to arrange, and is more susceptible to damage; an absorber incorporated into the material is present throughout the processing stages and its working life. Ultraviolet absorbers do in fact absorb ultraviolet light, and do so much more readily than plastics materials. The energy absorbed is released at a much longer wavelength in the infra-red region where it is harmless to the plastic. Generally those absorbers which are commercial products are capable of absorbing about 90% of the UV radiation of wavelength 350 mμ, in 0.1 mm thickness of plastic when incorporated at 0.2% (w/w absorber on plastic)(1). The absorption depends on the structure of the absorber and on the medium in which it is dispersed. A particular UV absorber may exhibit different values, and therefore have different efficiencies in various plastics. In

general, in less polar media the UV absorption is shifted towards the visible wavelengths. This shift can be as much as 5–10 mμ when the polar material cellulose acetate is compared with a polyester containing less polar styrene.

With a wide range of packaging materials available the choice of a particular one necessarily depends on many factors of which the major ones are :

(i) It must afford adequate protection from factory through to the last of the contents.

(ii) It must be reasonably priced.

(iii) It must be attractive and distinctive.

The protection afforded by the container should ideally include protection of the contents from fading or colour change due to daylight. This is easy where opaque containers are used, but the cosmetics industry offers many products which are attractive if seen and a transparent pack is then required. Glass has held sway for centuries but is heavy and fragile. Glass does, however, have some ultraviolet light absorbing properties, 1 cm thickness absorbs approx. 75% of the radiation at 350 mμ compared with 90% absorption at 0.1 mm thickness of a UV absorber treated plastic, but this is insufficient for any light-unstable product. To overcome this, the glass can be coated or wrapped in a UV absorbing film. A number of plastics materials fill all the requirements admirably, if they are UV protected.

The major materials are :

polyethylene, polypropylene	blow moulded bottles, injection moulded jars, tubs, films.
polyvinyl chloride (PVC)	tubes, bottles.
polystyrene	injection moulded jars and pots
cellulose acetate, cellulose butyrate	bubble packs, films.

No single UV absorber can be used for the whole of this range, and those commercially available number about thirty. Additionally, as research continues, new absorbers are introduced from time to time, either improvements on existing absorbers or new compounds, some specifically designed to stabilize a new polymer.

Although a large number of compounds absorb UV light there are a number of requirements which must be met before a particular compound can be considered as a plastics stabilizer.

(1) The absorption spectrum must be suitable, being high at wavelengths below 400 mμ with a sharp cut-off very near this limit, and a high transmission at longer wavelengths. A number of commercial materials have a slightly yellow colour due to absorption into the visible blue end of the spectrum.

(2) The compound must itself be stable to UV light. It must resonate readily, but not suffer any degradation.

(3) It must be stable to processing conditions, this may include resistance to oxidation by oxidizing agents and high temperature. Chemical inertness is also desirable.

(4) It must be compatible with high molecular weight materials so that it does not bleed out easily. Some compounds have long straight chain groups to "anchor" them in the polymer.

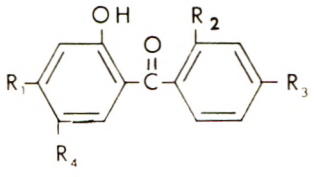
(5) It must have a low toxicity. Some UV absorbers are listed by the British Plastics Federation Toxicity Sub-Committee.

The most effective UV absorber is carbon black, but it has the disadvantage of always being the same colour; it has quite a wide use particularly for industrial and agricultural goods. The other absorbers are all organic compounds. From *Table II* and *Figure 3* it will be seen these fall into five classes :

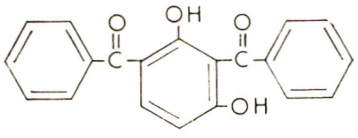
(i) Carbonyl group structures (benzophenones).
(ii) Carboxyl group structures (esters).
(iii) Benzotriazoles.
(iv) Substituted acrylonitriles.
(v) Organometallic compounds.

The majority of the commercial absorbers are in classes (i) and (ii), i.e. unsaturated ketones and esters which can be classified still more closely as 2-hydroxy benzophenones and salicylates (*Fig. 3, A and C*). In these two groups, a benzene ring carries an hydroxy group ortho to a carbonyl or carboxyl group. Hydrogen bonding between the hydroxylic hydrogen and the carbonyl oxygen gives a six membered chelate ring (*Fig. 3*), and it is this highly resonant structure which is responsible for the ultraviolet absorbing properties (2).

One carboxyl compound, resorcinol monobenzoate, appears to absorb more highly in the 400 mμ area of the spectrum than the others in this class. Actually the absorption curve changes during an initial "induction period" of UV exposure during which, it is believed, it rearranges to a



A



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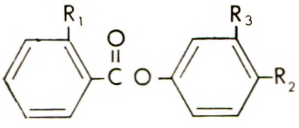

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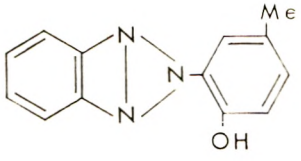

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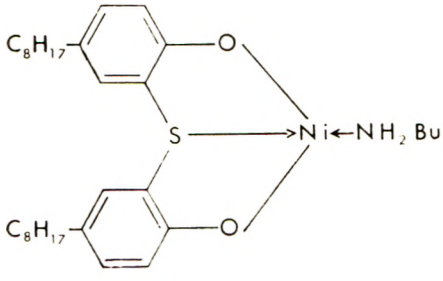
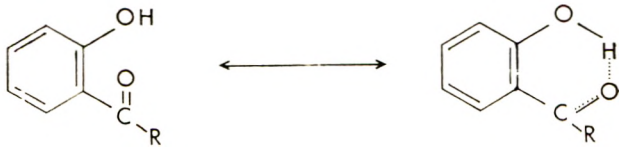


E

$[(CH_3)_2N]_3PO$

F

STRUCTURES



Formation of Resonant Chelate Ring

Figure 3

Table II

Chemical name	Trade name	Manufacturer*	
2-Hydroxy benzophenones			
2:4-dihydroxy benzophenone	*Uvinul 400* *Uvistat 12*	G.A.F. W.B.	A
2-hydroxy-4-methoxy benzophenone	*Cyasorb UV 9 Light Absorber* *Uvinul M40* *Uvistat 24*	ACCo G.A.F. W.B.	A
2-hydroxy-4-*n*octoxy benzophenone	*Cyasorb UV 531 Light Absorber*	ACCo	A
4-dodecyloxy-2-hydroxy benzophenone	*Inhibitor DOBP*	E.C.	A
5-chloro-2-hydroxy benzophenone	*Light Absorber HCB*	Dow	A
2:2'-dihydroxy-4-methoxy benzophenone	*Cyasorb UV 24*	ACCo	A
2-hydroxy-4-methoxy 4'-methyl benzophenone	*Uvistat 2211*	W.B.	A
2:2'-dihydroxy-4,4' dimethoxy benzophenone	*Uvinul D-49*	G.A.F.	A
dibenzoyl resorcinol	*Light Absorber DBR*	Dow	B

Structure**	Recommended for	Level	Toxicity LD_{50} ***
$R_1=OH$ $R_2=R_3=R_4=H$	polystyrene PVC cellulosics		
$R_1=OCH_3$ $R_2=R_3=R_4=H$	polystyrene PVC	0.2% 0.4–0.6 phr	5 g/kg
$R_1=OC_8H_{17}$	polyethylene LD and HD	0.3–0.5%	>10 g/kg
$R_2=R_3=R_4=H$	polypropylene	0.5%	
$R_1=OC_{12}H_{25}$	polyethylene LD and HD	1%	>25 g/kg
$R_2=R_3=R_4=H$	polystyrene PVC plastisol	0.5% 0.5%	
$R_4=Cl$ $R_1=R_2=R_3=H$	cellulosics PVC P.Vd.C.	0.5–3.0% 0.1–1.0% 0.5–3.0%	>10 g/kg
$R_1=OCH_3$ $R_2=OH$ $R_3=R_4=H$	PVC (plast.) lacquers cellulosics	0.1–0.2 phr <5% 0.5–1.0%	>10 g/kg
$R_1=OCH_3$ $R_3=CH_3$ $R_2=R_4=H$	PVC polystyrene cellulosics	0.2–0.3 phr 0.2–0.3% 0.2–0.3%	2 g/kg
$R_1=R_3=OCH_3$ $R_2=OH$ $R_4=H$	PVC PVC/PVA cellulose acetate	0.5–1.75 phr 0.5–2.5% 0.5–5.0%	
	polyethylene PVC P.Vd.C. cellulosics	0.5–2.0% 0.1–1.0% 0.5–3.0% 0.5–3.0%	> 4 g/kg

Chemical name	Trade name
Carboxyl Group Structures	
phenyl salicylate	*Salol*
4-*tert*butyl phenyl salicylate	*Light Absorber TBS*
4-octyl phenyl salicylate	*Inhibitor OPS*
resorcinol monobenzoate	*Inhibitor RMB*
Benzotriazoles	
2(2-hydroxy-5-methyl phenyl) benzotriazole	*Tinuvin P*
alkylated hydroxy phenyl triazole	*Tinuvin 326*
Substituted acrylonitriles	
	Uvinul N-35
	Uvinul N-539

Table II—*continued*

Manufacturer*		Structure**	Recommended for	Level	Toxicity LD_{50} ***
Dow G.S.	C	$R_1=OH$ $R_2=R_3=H$	polyethylene PVC P.Vd.C. cellulosics	0.5–2.0% 0.5–6.0% 1.0–6.0% 0.5–6.0%	> 1.5 g/kg
Dow	C	$R_1=OH$ $R_2=-C(CH_3)_3$ $R_3=H$	polyethylene PVC P.Vd.C. cellulosics	0.5–2.0% 0.5–6.0% 1.0–6.0% 0.5–6.0%	> 1.2 g/kg
E.C.	C	$R_1=OH$ $R_2=C_6H_{17}$ $R_3=H$	polyethylene polypropylene	1.0–5.0% 5%	
E.C.	C	$R_1=R_2=H$ $R_3=OH$	cellulose acetate cellulose acetate butyrate	1.0–2.0% 1.0–2.0%	
G	D		polyethylene PVC (plast.) polystyrene	0.05–0.2% 0.1–0.3 phr 0.2–0.3%	
G			polyethylene polypropylene	0.05–1.0% <1·0%	
G.A.F.			PVC lacquers	0.2–0.5 phr ca.5%	>16 g/kg
G.A.F.			polyethylene polypropylene PVC lacquers	0.1–0.5% 0.1–0.5%	

Table II—*continued*

Chemical name	Trade name	Manufacturer*	Structure**	Recommended for	Level	Toxicity LD_{50} ***
Organometallic						
(2,2'-thio-bis-(-4-*tert*octyl phenylato))-*n*butylamine Nickel II	*Cyasorb UV 1084* Light Absorber	ACCo	E	polyethylene HD and LD	>0.25%	
				polypropylene	<0.5%	
Others						
hexamethyl phosphoric triamide	*Inhibitor HPT*	E.C.	F	PVC (plast.)	1.5 phr	>6.4 g/kg
	Cyasorb UV 1376 Light Absorber	ACCo		polystyrene	0.25%	

**Manufacturers*

ACCo : American Cyanamid Company—Cyanamid of Great Britain Ltd.
Dow: Dow Chemical Company
E.C. Eastman Chemical Int. A.G.
G : The Geigy Company Ltd.
G.A.F. : General Aniline and Film Corporation, Inc.—Fine Dyestuffs and Chemicals Ltd.
G.S. : Graesser Salicylates Ltd.
W.B. : Ward Blenkinsop and Company Ltd.

***Structures* See *Fig. 3.*

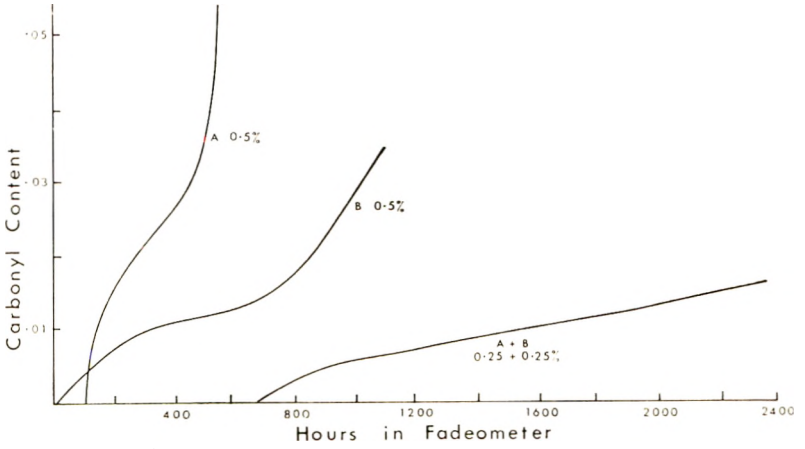
****Toxicities* are determined in rats or mice.

dihydroxy benzophenone structure. The nickel complex listed appears to be a poor absorber, but as it functions also as a free radical trap in oxidation reactions the overall performance is very good.

Plastics materials vary considerably in their susceptibility to UV light. In general, the thermosetting materials are quite stable due to their crosslinked structure, unlike thermoplastic materials, which are not crosslinked but consist of long straight or branched chains. In these, the stability is a function of the molecular weight, i.e. the higher the molecular weight the more stable the polymer. Double bonds in the chains, and some pendant groups, are the centres from which UV degradation starts. The mechanism of the degradation of various types of thermoplastics used in packaging, and the recommended UV absorbers are discussed below. Incorporation is usually by milling or tumbling resin powder with the absorber, then extruding to give a moulding powder or granules. The quantity of absorber added is usually within the range 0.01–5.0% but generally on a cost/performance basis the optimum is found between 0.2–1.0%.

The polyolefins to be considered are polyethylene of either high or low density, and polypropylene. Actinic degradation of these polymers leads to the formation, first of peroxides, and finally of carboxylic acid groups. The carbonyl content of the polymer can therefore be used as a measure of the degradation that has taken place. The best possible protection for polyolefins is channel black, but this restricts the colour to black. Of the UV absorbers listed the long chain benzophenones give the best results. 2-Hydroxy-4-*n*octoxy benzophenone, and 4-dodecyloxy-2-hydroxy benzophenone are the best of this class. The long straight alkyl chain provides sufficient compatibility with the long chain polymer, and hence bleeding out or blooming of the absorber from the polymer, in use, is averted. Of the two hydroxybenzophenones the octoxy derivative has the advantage of lower initial colour. Other absorbers tend to be more specific showing better results in either polyethylene or polypropylene ; in polyethylene films, for instance, the substituted acrylonitrile compounds, and in polypropylene, alkylated hydroxy phenyl triazole. Latest results show that if the nickel complex is used with another UV absorber, outstanding protection is afforded. A comparison of two, the nickel complex and 2-hydroxy-4-*n*octoxy benzophenone alone and in mixture, in polypropylene is shown in *Fig. 4.*

Polyvinyl chloride requires both heat and light stabilization. Metal salts, metallic soaps, alkylene oxide derivatives, or epoxy compounds are



Synergistic effect of combined stabilizers

Figure 4

the usual heat stabilizers. Both degradation mechanisms seem to be similar, with ultraviolet absorbers giving a three to fourfold increase in useful life against unscreened material. Degradation is by a free-radical mechanism whereby one atom of chlorine is released as HCl causing unsaturation ; this unsaturation leads to a loosening of the next chlorine atom, and so on along the chain in a zipper reaction. The strength of the C-Cl bond is approx. 78 k cal/mol (*Fig. 2*), and most damage is done to PVC by light of a wavelength 310 mμ having an energy content of 92 k cal/mol. The end result is a conjugated polyene structure which is coloured. Crosslinks can also occur across neighbouring chains which result in the polymer becoming brittle. Most of the absorbers listed are suitable for use in PVC. The heat stabilizers and plasticizers used have a bearing on the compatibility, so selection may be influenced by these factors. Plasticized PVC containing 2-hydroxy-4-*n*octoxy benzophenone shows minimal spotting after exposure in Arizona only after 3 years, compared to unprotected polymer which has severe spotting after 12–18 months. Synergism between the various stabilizers for PVC has been noted (3). When a UV light absorber is used in a system containing a barium cadmium chelator with an epoxy plasticizer, the protection afforded by the mixture is greatly in excess of that expected.

A combination of a tin compound as heat stabilizer with a short chain 2-hydroxy benzophenone or hydroxy methyl phenyl benzotriazole as UV

stabilizer is particularly good for rigid PVC. It is believed that alkyl tin compounds are UV light absorbers to some extent as well (4).

Polystyrene is pre-eminent for glass-like clarity and colour, coupled with lightness in weight and cheapness of an injection moulded plastic. On prolonged exposure to light, however, it yellows and crazes. This is caused by oxidation, not in the main saturated chains but in residual unsaturated low molecular weight units and monomer. As this oxidation takes place at the surface a powerful absorber, or a high level of absorber is required. Mono and dihydroxy benzophenones, particularly 2-hydroxy-4-methoxy benzophenone ; 2(2'-hydroxy-5'-methyl phenyl) benzotriazole, and the new *Cyasorb UV 1376* are the preferred UV absorbers. Some of the more powerful absorbers tend to absorb into the visible range, and so impart a slight initial yellow colour to the polymer. Where water-whiteness is necessary some care is required in the choice. Yellowness may be masked by the addition of a trace of blue or violet dye.

The cellulosics are a group of esters ; nitrate, acetate, propionate, butyrate or mixtures, usually plasticized, used in film form for window screens, bubble packs and wrappings, also in solutions, as lacquers. Ultra-violet radiation causes yellowing and embrittlement. Protection by the shorter alkyl chain absorbers with good solubility in polar solvents gives the best results. Resorcinol monobenzoate, benzophenones and 2(2'-hydroxy-5'-methyl phenyl)triazole in the organic esters, and the substituted acrylonitriles in both cellulose nitrate and acetate, are recommended.

(*Received : 15th September 1964*)

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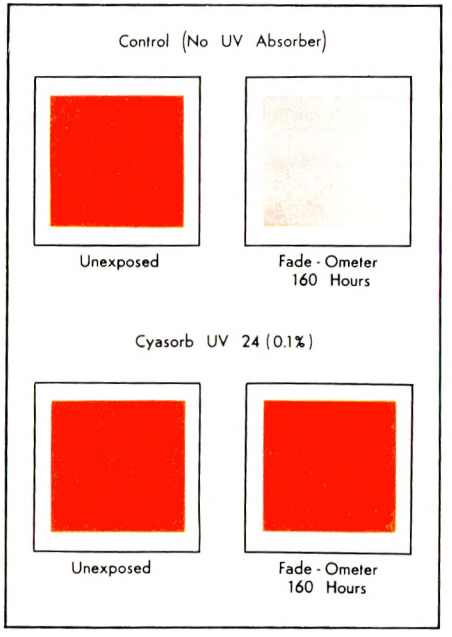
Introduction by the lecturer

About ten years ago, the Colgate-Palmolive Company took out 2 patents (5,6) in which they used 2:4-dihydroxybenzophenone, as an internal UV absorber in perfumes, toilet waters, and brilliantine. They found, and they claimed in their patents, that this gave complete stability to the colour of their products. After 20 hours' exposure in the fadeometer, a green dye faded completely. With as little as 0.005% of 2:4-dihydroxybenzophenone, however, there was virtually no change in the colour of the toilet water. In a brilliantine, they had an orange dye, a mixed dye, and

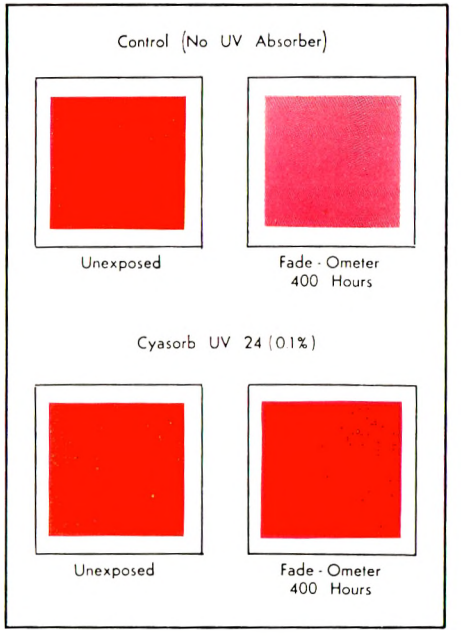
(5) U.S. Pat. 2,664,383.
(6) U.S. Pat. 2,678,901.

UV exposure of organic pigments 0.1% in polystyrene



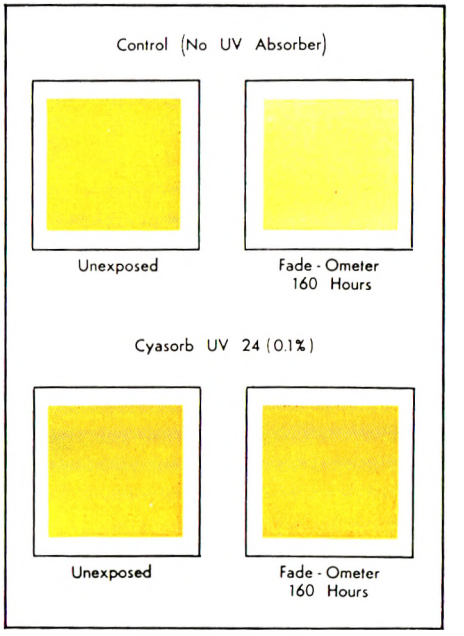
Red Lake C

Figure 5



Bonadur Red

Figure 6



Benzidine Yellow

Figure 7

unprotected this deposited a dark brown sediment, while the protected material for all practical purposes remained the same as the manufactured material.

The lecturer then displayed some UV exposed samples of hair shampoo, etc., in pairs, one sample in each case being wrapped in an UV absorbing film, the other being wrapped in a control film without absorber.

Figs. 5–7 demonstrate the effect on three different pigments shown treated and untreated in polystyrene. Exposure for 160 hr is a relatively short time; ordinary plastics materials are normally exposed for something of the order of 1000 hr. This indicates that the rate of fading is quite rapid without some form of protection.

Polypropylene is a flexible plastic and is used where flexibility is particularly required. Polypropylene, however, is susceptible to UV degradation, and it is therefore advisable to use a UV absorber.

The lecturer then folded two pieces of polypropylene. The unprotected piece cracked in half immediately, the UV stabilized piece was folded flat on itself without any damage.

The untreated material shows stress-cracking in the area adjoining the fracture while the protected material is unharmed. The absorber used in this polypropylene is 2-hydroxy-4-*n*octoxybenzophenone, in which the long alkyl chain acts as a "molecular anchor", thereby increasing the compatibility of the absorber in the polypropylene by threading its way through the long linear chains of the polypropylene molecule.

DISCUSSION

MR. R. J. MOTZ: Could you say whether food could be wrapped in transparent films in which some of these agents are incorporated without any danger of some materials being leached out into food (a) containing fat, and (b) without fat? Could this be objectionable?

THE LECTURER: It has been found that the 2-hydroxy-4-methoxybenzophenone is extracted from films almost to an unmeasurable extent by oil. A number of UV absorbers have been, or are being, classified for toxicity quotients by the British Plastics Federation: 3 are listed in the Second Report of the B.P.F. Toxicity Sub-Committee.

MR. R. J. MOTZ: Does it mean that some of these materials are included in the permitted list or excluded from it?

THE LECTURER: The B.P.F. ratings relate to ingredients of plastics materials which are used for food wrapping only. For an ingredient to be acceptable it must be shown to be without any toxic effect when ingested at a level well above that ever likely to occur in practice. Further, any plastics ingredients likely to be extracted into food must not contravene the Food and Drugs Act, 1955.

You mentioned the use of UV absorbers in food wrapping materials. It has been shown that meat, cut ham, cut bacon, etc., laid out in some of these refrigerated displays tend to change shade or colour and look rather unappetising. Most of the fading is due to UV light; it would therefore be possible to preserve the colour by wrapping such meat in a UV protective film.

DR. T. J. ELLIOTT: In the cosmetic industry there are two products which are still prone to UV degradation, viz. perfumes, and coloured aqueous or aqueous alcohol solutions in bottles.

Is there any practical method of incorporating UV absorbers in the glass, either during manufacture, or by coating the glass afterwards?

Do you know of any work, in co-operation with perfume manufacturers, to incorporate UV absorbers into alcoholic solutions ?

Is there a water-soluble UV absorber which can be incorporated into coloured solutions to increase the shelf life of the normal, very rapidly fading, permitted colours ?

THE LECTURER : These organic UV absorbers cannot be incorporated into glass. They will be destroyed before the glass is fully melted. Some work was done by the British Glass Industry Research Association on various metallic oxides to improve the UV absorbence of glass, but so far as I know none of their results reached the level which can be achieved by organic absorbers dispersed in organic film.

It is quite feasible to over-wrap a glass bottle in a UV absorbing film.

I have already mentioned the incorporation of UV absorbers into the perfume itself (5,6) covering the use of 2:4-dihydroxybenzophenone.

A UV absorber for use in a product which will be applied to the skin, should not possess any toxic or dermatological hazards. Most absorbers are sufficiently soluble in alcohol to be used in perfumes, but for aqueous systems a special water-soluble absorber would have to be used, such as 2-hydroxy-4-methoxy-5-sulphobenzophenone ($R_1 = OCH_3 : R_2 = R_3 = H : R_4 = SO_3H$) and sodium 2:2′-dihydroxy-4:4′-dimethoxy-5-sulphobenzophenone ($R_1 = R_3 = OCH_3 : R_2 = OH : R_4 = SO_3Na$) (*Fig. 3A*).

MR. H. F. FROST : I noticed how thick the film is on the samples which are being circulated. In fact much thicker than I would regard as suitable for over-wrapping in the normal way. What is the relationship between the concentration of inhibitor required, and the thickness of the film ?

THE LECTURER : Fortunately there is a simple, straight-line function between these two. If you halve the thickness of the film, you double the concentration of the absorber and get the same effect.

MR. H. F. FROST : In that case, what is the maximum amount that can be incorporated in a film ?

THE LECTURER : Owing to the many factors involved it is impossible to give a direct answer. You must carry out your own experiments with different types of film materials, and the different absorbers. For instance, if you were using a polyolefin film, then the absorber with the long alkyl chain would be better than an absorber with a short chain.

MR. A. HERZKA : Do I take it that different gauges of film, incorporating different concentrations of absorber, are readily available for experimental purposes ?

THE LECTURER : No. Only some material is available commercially.

DR. J. A. MYERS : Polypropylene becomes brittle on treating with γ radiation. What is the effect of γ radiation on UV absorbers, and on the toxicity of polypropylene and other plastics used for plastic tubing ? Do the plastics listed in *Table I* become more toxic on storage in light ? What toxic products, if any, would be leached out from these plastics if used for tubes, bags, etc., conveying human blood, e.g. plastic heart-lung units, artificial kidney units, hypodermic syringes, etc. ?

Do blood, and drug solutions remove toxic materials from these plastics after they have been stored in light ?

THE LECTURER: I am sorry, I have no data whatsoever. P.V.C., which gives degradation products in UV light, would obviously be unsuitable. Polyolefins, as far as we know, tend to cross-link, and therefore become more insoluble. Presumably they would therefore be better.

The amount of UV absorber extracted is virtually below the level which can be measured, and a polyolefin containing a UV absorber, should therefore provide your safest container.

MR. M. S. PARKER: Can you tell me anything about the loss of the absorbers, or their changes, if you heat sterilize a complete plastic package containing them ?

THE LECTURER: The amount of heat sterilization which the majority of thermoplastics can undergo is not very great. These are preferably sterilized by γ radiation. As the UV absorber will be incorporated at a very early stage of manufacture, or in the processing of the polymeric material, it will have to be heat-stable above the melting point of the polymer.

MR. J. D. CHESHIRE: Can you comment on the relative merits, and the relative economics, of using antioxidants rather than UV absorbers in the product if faced with a deterioration which is known to be due to photo-oxidation, and one is unable to use a plastic film on the outside of, for instance, the glass container ?

THE LECTURER: You would do very much better with both. The antioxidant will react with the oxygen present in the vessel, and is therefore expendable to a certain extent. You will obtain a very much more stable product if you can reduce the workload on your antioxidant, by cutting out the initiation stage with the UV absorber.

DR. A. HUNGER: Is not glass quite a good UV absorber by itself ?

THE LECTURER: Not by comparison with the deliberately designed UV absorbers. The absorption is less than 50% at wavelengths greater than approx. 340 mμ.

MR. K. C. JAMES: It is observed that all the light absorbing materials described in your paper have a hydroxyl group ortho to the ketone, and the other ortho position vacant. Are these essential structural requirements ? Is the second benzene ring also necessary.

THE LECTURER: *Fig. 3* shows the formation of the ring structure which resonates. It is this structure which is responsible for the activity of both the 2-hydroxybenzophenones and the salicylates. The ortho position on the second ring does carry an hydroxy group in quite a number of absorbers. In 2:2′-dihydroxy-4-methoxy benzophenone, the second OH group increases the UV absorption when compared with the monohydroxy compound. The spatial effect of the second benzene ring probably helps to locate the carbonyl group in a suitable position for chelation with the OH group.

MR. N. J. VAN ABBÉ: I would like to refer to your method of classifying toxicity in *Table II*. I think it is unlikely that the customers eat the bread wrapping with the bread in large quantities, and I am rather doubtful of the value of acute toxicity as an indicator of the toxicity of compounds used in this way. I suppose it would have been difficult to tackle this in any other manner, but it might be valuable to give an indication of how you rate LD_{50} values ?

I feel that in relation to one of the accepted types of classification, anything

over perhaps 3 or 5 g/kg would be regarded as virtually nontoxic. Does the British Plastics Federation require chronic toxicity information in drawing up its classification ?

THE LECTURER : Your first remark is perfectly true ; one does not eat the wrapping with the bread, in spite of the old joke about the *Cellophane*-wrapped sandwiches. The B.P.F. ratings are based on the maximum dose that will exhibit no toxic effect on long-term feeding trials, and the toxicity factors quoted are a function of this, and of the extractability of the particular material into food. Only the acute toxicities are quoted in the trade literature.

A MEMBER OF THE AUDIENCE : Could you give us some idea of the cost of including these UV absorbers in the plastics ?

THE LECTURER : The cost of the absorbers varies ; they are generally relatively expensive but are used in quite small quantities. I think the additional processing costs will be quite low. I believe that the added cost is something of the order of 1d, 1½d, or 2d a lb.

MR. P. H. MARRIOTT : Is there any application of UV absorbers in the coating of tablets to preserve the colour, and prevent fading ? Are there any edible ones which can be used ?

THE LECTURER : It is possible to incorporate an absorber in a gelatine capsule but a full toxicological investigation would be necessary, the cost of which may never be justified economically.

Book reviews

CHROMATOGRAPHIC REVIEWS, VOLUME 6. M. Lederer (Ed.). Pp. viii + 219 + Ill. (1964.) *Elsevier Publishing Company, Amsterdam/London/New York.* 70s.

A review, by definition, sets out to summarize the significant advances made in a particular, usually specialist, field; it should extract and assess the latest developments from a heterogeneous cascade of both directly relevant publications and incidental references. When such a review is part of a series, and therefore surveys progress since the previous volume, it must be measured against a double standard: not only the criteria on which the series was founded but also any novel character in the period under review.

In 1958, Dr. M. Lederer (Rome Institute of General and Inorganic Chemistry) consented to edit a series of reviews, each volume covering the published applications of various forms of chromatography in the preceding year. At the time, shortly after the half centenary of Tswett's first chromatographic column, the generic term "chromatography" had already become so polyvalent as to be almost meaningless without specific qualification. The earlier volumes of the series, then, attempted to summarize progress with particular chromatographic techniques, especially those described in the previous year in *J. Chromatography*, of which Dr. Lederer is in fact the editor. In the last two Reviews, this original ambit has unavoidably been broadened; the current number contains eight specialist essays, including topics in the congeneric fields of electrophoresis and ion exchange. Three had been given as lectures whilst the other five are original contributions surveying several years of progress in a particular technique or application. For this reason, although the date line is May 1964, most of the contributors cite references over the period 1950–62.

In the first review, G. S. Learmonth (Birmingham College of Advanced Technology) undertakes a broad survey of the apparatus commercially available for gas chromatographic analysis. He deliberately addresses himself to the general analyst rather than to the tiro specifically concerned

with the development of methods employing gas-liquid chromatography (GLC) or gas adsorption chromatography (GAC). Specific items of equipment for the different stages of the GLC or GAC processes are assessed and useful Tables classify the main features of the great majority of available instruments, stationary phases, detectors, recorders and ancillary equipment, e.g. for integration or temperature programming.

Three Czech workers, Z. Deyl, J. Rosmus and M. Pavliček, contribute a timely and comprehensive review of Centrifugal Paper Chromatography, in which the analytically disadvantageous slowness of the mobile phase in "classical" (i.e. as old as the 1950's !) paper partition chromatography (PPC) is accelerated by application of a centrifugal force. The principles of this fundamental advance were first enunciated by Caronna in 1955, but the authors of the review have contributed notably to its development. Individual types of apparatus differ mainly in the means of delivery of the mobile phase to the filter paper, e.g. eccentrically, by a central needle from a reservoir or from a rotating chamber. Reference is made to quantitative interpretation and to the separation of a variety of natural products.

A Finnish biochemist, J. J. Saukonnen, succinctly reviews the highly specialized techniques that have been developed for the separation of metabolically significant nucleotides, i.e. nucleoside phosphates of relatively small molecular dimensions. The methods include ion exchange (on resin, cellulose or paper), conventional PPC, electrophoresis in one or two dimensions or in thin layers, "normal" Thin Layer Chromatography (TLC), gel filtration, charcoal adsorption and GLC. Altogether 245 references are given to the main paper and a similar number are cited in appended schemes and Tables of applications.

Another specialist application, the separation of iodoamino and related compounds by PPC is surveyed by L. G. Plaskett (University of Edinburgh Medical School). Previous reviews have emphasized the special suitability of PPC for this task and tabulated a great deal of R_F data or reviewed radiographic techniques, all of which permit this essay to concentrate on the selection of solvent systems and the chromatographic behaviour of particular compounds, although reference is necessarily made to sample preparation and detection methods–which include neutron activation analysis !

Gunter Zweig's review of Chromatographic Techniques for Pesticide Residue Analysis is based on his address to the 5th International Pesticide Congress in London, July 1963. In residue analysis, microgram (or even nanogram) amounts of pesticides have to be determined in the presence of

up to 10^9 excess of vegetable or animal substrate. This paper deals with PPC specifically for chlorinated, organo-phosphorus, carbamate and miscellaneous pesticides, and then surveys the application of TLC and GLC and polyvalent combinations of these techniques. Column chromatography is not regarded as a discrete method of residue analysis but rather as a preliminary clean-up as, for example, in the Laws and Webley omnibus procedure for organo-phosphorus compounds. A number of paper and gas chromatograms of diagnostic interest are illustrated and quantification methods are outlined. It should be observed that the review is largely based on American experience ; the majority of references cited are of American origin whilst significant European papers are not mentioned ; this is one drawback of reprinting a Congress lecture out of its context.

Both ion exchange (on a resin bed or column) from aqueous solution and counter-current extraction with organic solvent from an aqueous phase, are well established techniques. In his Rome postgraduate lecture, E. Cerrai (Milan) discussed the relatively recent development of ion exchange into an immiscible liquid phase impregnated on an inert support. The extraction kinetics are basically similar to those for conventional ion exchange at a liquid/solid interface but without some of the electrostatic field complications of the latter. The original requirement for a continuous extraction process was industrial and it has been applied to many of the separations in the nuclear industry. More recently, a number of anion exchange liquids have been adopted for laboratory analytical applications. Special attention is given to supports impregnated with tri*n*octylamine and bis-(2-ethylhexyl)phosphoric acid. Numerous examples are given of elution curves for a variety of systems and supports, with coloured and half-tone illustrations of the chromatograms achieved.

G. Nickless and G. R. Marshall (Bristol University) considered the synthesis and application of selective ion exchangers and polymeric chelate compounds. Such inorganic polyelectrolytes are of two types : Linear metal-anion chains and recurring intermolecular polydentate systems. Although necessary in a short review, the compression, with which for example synthetic routes for a wide variety of compounds are summarized, makes for difficult reading ; this article contains a wealth of information and it requires careful digestion if it is usefully to be assimilated. Nevertheless the authors effectively draw attention to the great potential offered by these new materials that occupy a position intermediate between metals and non-metallic substances.

Another lecture translated for this volume was given by E. Blasius

(Charlottenburg Technical University, Berlin). With his collaborator W. Preetz, he is concerned with the application of paper ionophoresis and electrochromatography to the study of the equilibrium conditions for metal complexes in solution–a subject near to the heart of the general editor of this Review series. General principles are briefly enunciated and suitable apparatus is described and illustrated. Particular attention is given to the identification and interpretation of the hydrolysis products of the complexes of the group VIII metals ; numerous examples are shown of diagnostic absorption spectra.

Such is the exponential increase in the scientific literature and concomitant rationing of the demand on the analyst's time that the editor of such a review has a heavy responsibility. It may fairly be conceded that Dr. Lederer has again supplied solid but in most cases palatable surveys of techniques, some part of which could supply an application we severally require. In view of the vogue for separation by TLC, the absence of a consolidating survey in the present volume may be regretted ; but Dr. Lederer refers to a concurrent publication, edited by G. B. Marini-Bettolo, which collates a number of reviews covering all aspects of this very fecund field. It is hardly necessary to add that the present volume continues the high Elsevier standard of printing. Diagrams, spectra and structural formulae are neatly and accurately delineated, whilst a wide variety of chromatograms are well produced in monochrome or colour. G. F. PHILLIPS.

THIN-LAYER CHROMATOGRAPHY. G. B. Marini-Bettòlo (Ed.). Pp. xi + 232 + Ill. (1964.) *Elsevier Publishing Company, Amsterdam/London/New York.* 65s.

Cosmetic chemists who have recognized gas-liquid chromatography (GLC) as an analytical necessity will be aware of its main limitation, viz. non-volatility of all or part of the sample. Thin-layer chromatography (TLC) will overcome this limitation, and the multiplicity of applications of this expanding technique is well demonstrated in the volume under review.

A Symposium held in Rome in 1963 is presented in 26 papers, of which two are in French, four in German, and the remainder in English. The contents are not clearly classified, although descriptions of techniques are mainly found in the first half of the book while the second half is concerned with specialist applications. An extremely comprehensive eight-page index establishes the value of the book for any analyst's reference library.

Well chosen as the first paper is Professor Stahl's review of the develop-

ment and application of TLC. It provides an insight for the beginner and will convince any sceptical chemist of the value of TLC, besides whetting the appetite to read more of the specialist techniques and applications. It is a pity that this review is marred by the omission of references. Throughout the rest of the book, however, the page on which appropriate references are to be found is indicated by footnotes ; a feature to facilitate the task of literature searching.

Stationary phases other than Silica gel G are reported in three papers. Cellulose ion-exchangers have been applied to analyses of food colours, metal ions, organic acids, carbohydrates, and nucleic acid derivatives ; loose layers of alumina are described as a technique for many separations ; and the scope of reversed phase TLC on starch is outlined. Special techniques include thin-layer electrophoresis (TLE) of phenolic compounds, naphthols, amines, amino acids, dyestuffs and iodate/periodate mixtures. Centrifugal TLC is advocated for analysis of dyes and 2,4-dinitrophenylhydrazones within 5–10 min, while mass spectrometry has been used as an ancillary technique in the elucidation of steroid structures.

The paper on lipid analysis by Padley deserves special mention for its interest to cosmetic chemists investigating fats from skin and hair. It is an exceptionally well-classified and readable review covering all recent developments of technique and application of TLC for the separation of lipids. Another author, describing the separation of natural and synthetic odorants, points out the advantage that heating is not necessary for TLC, in contrast to GLC or distillation ; but he does not mention that his separations of menthol isomers could be more readily achieved by GLC Not until analysts accept TLC and GLC as being complimentary, rather than competitive techniques, will their real value emerge.

Common interests of food and cosmetic chemists are concerned in a paper on food colour chromatography, while biochemists and pharmacists will find five papers discussing steroids and three on alkaloids. Proteins and peptides are analysed by TLE or TLC on Sephadex and the use of TLC in medical laboratories is further demonstrated by investigations of aminoaciduria and the analysis of phospholipids of mitochondria and tissue sections.

Other applications of the technique are represented by papers on analyses of metal ions and polynuclear hydrocarbons and on determination of oxime configurations. Obviously, a technique as versatile as TLC, with many avenues yet unexplored, should be a feature of any serious analytical laboratory, and this book is a valuable reference for the beginner and expert alike. J. D. CHESHIRE.

STRUCTURE AND ACTIVITY OF ENZYMES. Editors: T. W. Goodman, J. I. Harris and B. S. Hartley. Pp. viii + 190 + Ill. (1964.) *Academic Press, London and New York.* 37s. 6d.

Accumulation of knowledge of amino acid sequences in proteins appears to be verging on an exponential phase of growth. At this symposium, structures of two of the smaller enzyme molecules were known, and work on others was proceeding apace. In addition, new methods of specific substitution of side chains in proteins are steadily giving real structural meaning to the previously nebulous terms of the enzymologist such as "active centre."

The papers at this symposium were divided into four sections. Under the heading "Ribonuclease" were papers describing its structure and active sites, and theories of mechanism of action. In the next section, "Chymotrypsin," the final points of disagreement between laboratories concerning the structure of this enzyme were discussed. In both these sections studies on crystal structure were also described.

The third section, "Active Sites," is concerned with methods of determination of the active centres of a number of different enzymes. Esterases, thiol dehydrogenases, B-6-containing enzymes, carbonic anhydrase, alcohol dehydrogenase, and the glucose transport system of human erythrocytes are among the enzymes discussed.

Finally, a section on "Haemoglobin" illustrates the use of kinetic studies in understanding mechanisms of action.

The book is useful in bringing together the methods currently in use in this area of biochemistry, and provides, in addition, a review of the state of knowledge concerning enzyme structure. It is interesting reading for chemists and biochemists wishing to keep up to date in this fundamental field. There is a good index, and many of the papers carry extensive references. Others may find, however, that the absence of summaries is a hindrance to easy reading. B. G. OVERELL.

PROGRESS IN THE BIOLOGICAL SCIENCES IN RELATION TO DERMATOLOGY.2. Editors: A. Rook and R. H. Champion. Pp. xiii + 499 + Ill. (1964.) *University Press, Cambridge.* 130s.

A course for clinicians was held in Cambridge in 1963 dealing with recent advances in the biology of skin. This was the second such course, a similar one having been held in 1958. As far as possible, topics which were dealt with in the first course were excluded the second time.

The second course of lectures, which were delivered by research workers active in their respective fields, has been grouped in this volume under ten headings. These are "The Functions of Connective Tissue," "Ageing of Skin," "Regeneration and Repair," "Subcutaneous Fat," "Keratinization," "Percutaneous Absorption and the Epidermal Barrier," "Hair," "Cutaneous Circulation," "The Physiopathology of Bulla Formation," and "Some New Techniques in Dermatology Research."

Considerable interest is shown in connective tissue. Collagen is discussed from the point of view of structure and metabolism by R. D. Harkness, and its degradation by D. A. Hall. One reason for this interest is illustrated, for instance, by F. J. Ebling, who, in his paper on the hair follicle, suggests that variations in the collagen in the skin may influence follicular activity. Similarly Helen Muir, in discussing mucopolysaccharides in the dermis, describes stimulation of hair growth by injection of mucopolysaccharides.

The ageing of connective tissue is discussed by R. E. Tunbridge. A. Comfort gives an interesting paper in which he discussed theories of ageing mechanisms. This study is in its infancy, however, and it is disappointing for the cosmetic scientist to learn that little progress has yet been made in understanding the mechanism of changes in skin which occur with age and which are visible to the naked eye.

The section of percutaneous absorption has much to interest those who are concerned with toiletries. The epidermal barrier is discussed by I. H. Blank and R. J. Scheuplein. R. B. Stoughton deals with methods of measurement of percutaneous absorption; permeability in relation to structure is discussed by R. T. Tregear, and with reference to steroids by A. W. McKenzie. Finally, C. F. H. Vickers presents the epidermis as a reservoir for topically applied agents, an aspect which obviously has great significance in the development of toiletry products with prolonged action, such as deodorants.

It is inevitable in a book of this type that the quality of the contributions varies considerably. Some contributors have produced reviews, some have given summaries of their own original work, and some have given general discussions of theories and interpretations. The papers carry a variable number of references. Some lists are very extensive; some are non-existent. The index is too small to be of any great use in a volume of this size, but the book is otherwise well produced.

Despite the audience for which it was intended, the book does not have a pronounced clinical flavour, and it provides interesting and stimulating

reading for those who have some knowledge of skin biology. Taken as a whole it fulfils very well its purpose of providing a picture of what is currently going on in its chosen fields of research on skin. B. G. OVERELL.

THE DYNAMICS OF RESEARCH AND DEVELOPMENT.

E. B. Roberts. Pp. xxii + 352 + Ill. (1964.) *Harper & Row, Inc., New York/Evanston/London.* 82s.

The problems of managing large research and development resources are so relatively new that a book of this kind, stemming as it does from the Industrial Dynamics studies that have been carried out at Massachusetts Institute of Technology over a number of years past, must be welcomed even though its value lies more in making the nature of the problems explicit than it does in solving them.

While writing this book, Roberts's thinking has, probably inevitably, been overwhelmingly influenced by the enormous expenditures on research and development contracts of United States Government agencies such as the National Aeronautics and Space Administration, and the book is an heroic attempt to bring all the factors that produce success or failure in one of these vast projects within the compass of some 240 mathematical equations which can then be fed into a computer for solution. The aim is not to provide a means of simulating any particular situation for the purpose of forecasting success or failure, but rather to simulate a general situation so that the effect of changes in various factors can be studied. Such a procedure can only be of more than academic interest if the factors studied can be identified and modified in real situations. For example, it is not too surprising to learn that the parameter "Quality of [Contracting] Firm" has a marked influence on "Project Cost" and the "Completion Date," but what is not clear is how one could assess the qualities of different competing firms and so make use of this information. Even if this parameter could be measured there is no assurance that it would act in real life as it does in Roberts's model because this, though plausible, is not empirical. It seems, then, that Roberts's "management laboratory" approach, which he regards as a logical next step to the use of wind tunnels, is based on a fallacy. The whole virtue of a wind tunnel is that

(1) there is a known relationship between the parameters of the model and those of the full-scale article;

(2) this relationship is measurable; and

(3) the effect, both qualitative and quantitative, of changing a parameter of the full-scale article can be deduced from a knowledge of what

happens to the model when the corresponding parameter is changed by a corresponding amount.

If these conditions were met by Roberts's model, he would have no need to talk about management laboratories. He would measure the parameters in the real situation, feed them into his equations, and so make predictions. Insofar as they are not met, Roberts's model becomes a toy, and his management laboratory a management game – a useful teaching device, but still a game.

The book is written in two parts; the first deals with the setting-up of the mathematical equations for the model, each chapter starting with a verbal description of one aspect of the total problem and finishing with equations expressing the same thought; while the second part of the book gives the results of computer runs under various input assumptions about the project, the contracting firm, and the customer together with a discussion of these results. The equations are all written in a fairly simple computer language called DYNAMO for which compiler and simulator programmes are available for use on IBM 709 and 7090 machines. A typical listing of the programme is reproduced in an appendix, and there is a five and a half page index. K. T. BOYD.

Society of Cosmetic Chemists of Great Britain

ANNUAL DINNER AND DANCE

Sir Owen Wansbrough-Jones, K.B.E., C.B., M.A., Ph.D., F.R.I.C., Executive Vice Chairman of Albright & Wilson Ltd., was Guest of Honour at the Society's Annual Dinner and Dance held at the Connaught Rooms on 13th February.

Mr. A. Herzka, President of the Society, proposed the toast of the guests and in so doing drew attention to the fact that several of them represented Societies and Institutions with whom the Society had a close relationship. Mr. Herzka mentioned the Diploma Course, the standards of which had been progressively raised. It was now hoped to recognize this by the proposed alteration in the Rules. The success of the Society's joint symposium with the Pharmaceutical Society and its election to membership of the Parliamentary and Scientific Committee were encouraging signs of progress.

In introducing the Guest of Honour, the President referred to Sir Owen's achievements in industry, and also to the Society's interest in his chairmanship of both the Colloid and Surface Chemistry Group of the Society of Chemical Industry, and of the Council of the British Industrial Biological Research Association.

Sir Owen Wansbrough-Jones replied to the toast and in alluding to the historical aspect of cosmetics referred to a sermon devoted to the subject and given in 1576. He stressed the importance of a scientific basis for the cosmetic industry and disagreed with those who could only emphasize the safety of natural products while considering synthetic materials as harmful. It was also important that we should know with greater certainty that cosmetic ingredients have definite effects. In conclusion he welcomed the existence of a society, the members of which were applying scientific study to what had previously been an art, but stressed that the artistic aspect was still important.

Among other guests present with their wives were Mr. W. Howie, M.P.,

Mr. Will Howie, M.P., being welcomed by the President; Mrs. Howie on far right.

From left to right: Sir Owen Wansbrough-Jones, Mrs. Herzka, and the President.

From left to right: Mrs. May, Mr. A. Stafford May (Chairman, Toilet Preparation Federation), the President, and Mrs. Herzka.

The President's table.

Facing page 246

a Government Whip and Member of the Parliamentary and Scientific Committee, Mr. C. W. Maplethorpe, President – The Pharmaceutical Society of Great Britain, Mr. A. Stafford May, Chairman – Toilet Preparations Federation, and Mr. J. B. Wilkinson, President – International Federation of Societies of Cosmetic Chemists.

ALTERATION TO RULES

A Special Meeting was held at the Royal Society of Arts, John Adam Street, London, W.C.2, on Thursday, 25th February 1965. Twentytwo Members and Associates were present.

The Chair was taken by the President, Mr. A. Herzka, who explained that the Council was proposing alterations to Rule 3 because the minimum requirements for entry into the Diploma course had been raised, and thus the Diploma itself now represented a higher educational standard than would appear to be evident from the existing Rules.

The Council also felt that because of the importance of the Diploma course, the Hon. Education Secretary should be a Member of Council with full voting rights.

After some discussion, two motions were put. The motion concerning alteration to Rule 3, ii (c), (d), and iii was put to the vote and carried unanimously. The motion to alter Rules 11 and 41 was put to the vote, and carried by 21 votes in favour, with one vote against.

MEDAL LECTURE

The Council has agreed to institute an Annual Medal Lecture, and it was decided that

> "the recipient of the Annual Medal shall be a leading personality who has made an outstanding contribution to science, public life or the arts. The lecture shall be on cosmetics or allied subjects."

The 1965 Medal Lecture entitled *The hormonal background of the skin*, will be given on Wednesday, 14th April by Professor Sir Edward Charles Dodds, M.V.O., F.R.S., F.R.I.C., Courtauld Professor of Biochemistry, University of London.

Admission by tickets, obtainable from the General Secretary.

FILM EVENING

A Film Evening will take place on Thursday, 13th May, at the Royal Society of Arts, John Adam Street, London, W.C.2, at 7.30 p.m.

SYMPOSIUM ON PHYSICAL METHODS

A symposium on *Physical Methods* will take place in Bristol on the 16th November 1965. The following papers will be discussed:—

"Application of moving bed chromatography to preparation of pure sample in the cosmetic industry."

"Fluorescent antibody techniques."

"Particle sizing."

"The relation between structure and properties in plastics used in packaging."

"Gas-liquid and thin layer chromatography, infra-red spectroscopy."

"Spectrophotometric methods for the rapid evaluation of the inactivation of anti-microbial agents."

"Rheological studies of new cream bases with the Brookfield Lynshro-Leihur Viscometer."

"Rheological topics in relation to cosmetics."

"Spectral slit width and other sources of error in UV spectrophotometry."

"Infra-red spectroscopy of aqueous detergent solutions."

There will also be a demonstration of various types of physical apparatus arranged by Bristol University. Registration forms giving final details will be available in June, from the General Secretary.

FUTURE SYMPOSIA

A Symposium on **Colour** will take place in Eastbourne, Sussex, during the week commencing 25th April 1966.

A Symposium on **Product Testing** will take place in Leamington Spa, on the 16th November 1966.

ANNUAL GENERAL MEETING

This will take place on Monday, 24th May, at 7 p.m., at 55 Park Lane, London, W.1.

4TH I.F.S.C.C. CONGRESS

The 4th I.F.S.C.C. Congress will take place in June 1966, in Paris. Anyone wishing to submit a paper should contact the Société Française de Cosmetologie, Maison de la Chimie, Rue Saint Dominique, Paris VIIe, France.

Published on behalf of the Society of Cosmetic Chemists of Great Britain by Pergamon Press, Ltd., Headington Hill Hall, Oxford. Printed and Bound by Cheltenham Press Ltd., Swindon Road, Cheltenham and London, Great Britain.