Journal of the Society of Cosmetic Chemists

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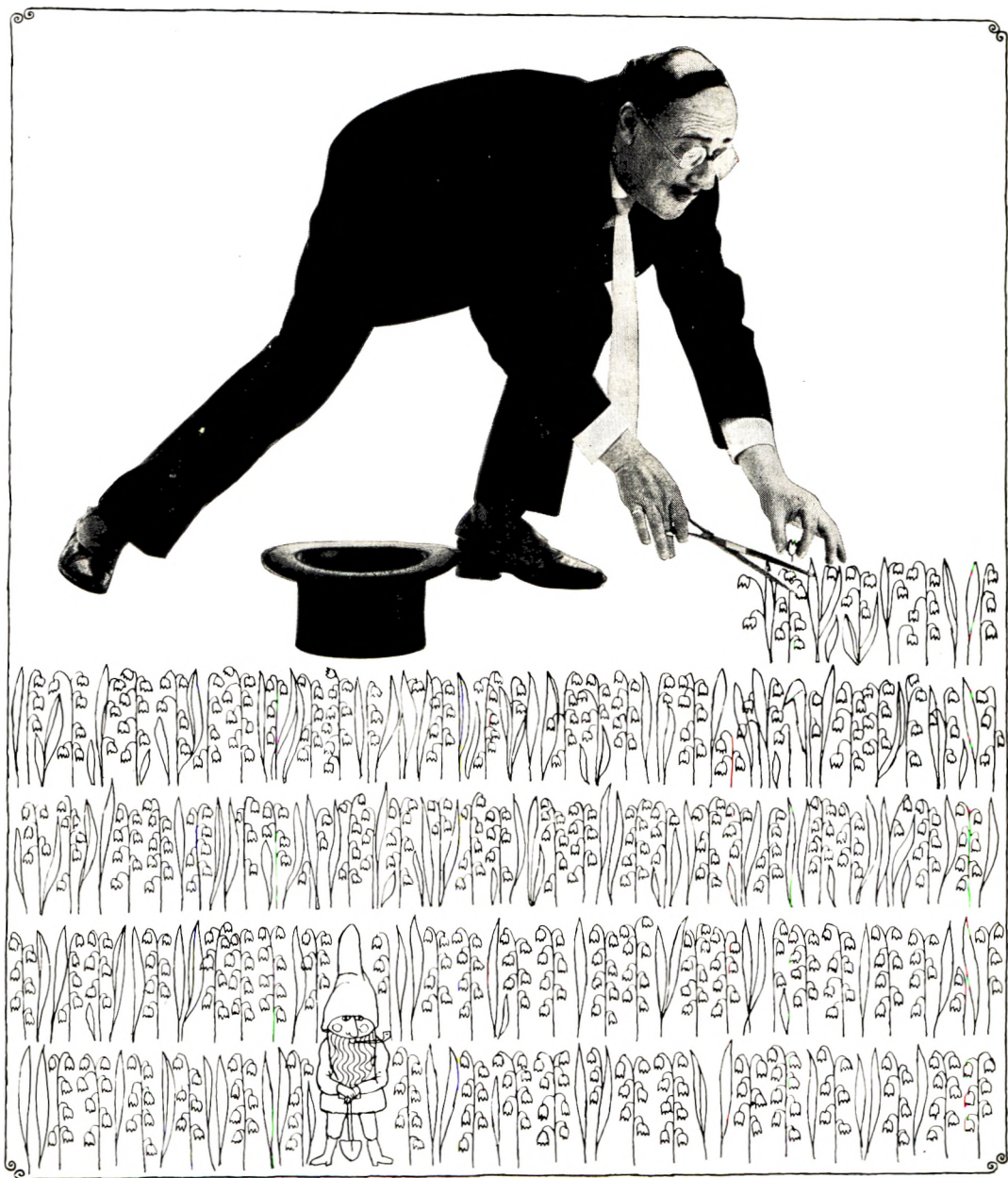
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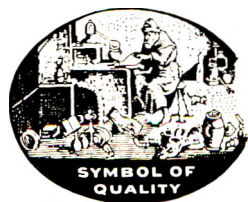
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Research Section : contains original research articles that will keep toxicologists and other scientists abreast of the most recent advances in the field.

Review Section : provides information on papers dealing with the biochemical, pharmacological, toxicological, medical and veterinary aspects of the subject.

Information Section : divided into the following sub-headings—Legislation : deals with world changes in legislation relating to food additives and contaminants, cosmetic and toilet preparations, etc.
Articles of General Interest :—discussions of more general topics and of papers appearing in other journals reflecting progress and opinion in toxicology.
Toxicology : Abstracts and Comments :—These are more than mere digests of papers published throughout the world ; they are invariably more lengthy than orthodox abstracts, containing all the salient facts to be found in the original article plus the comments of the Editor and his colleagues.

Summary of Toxicological Data

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ANY RESEMBLANCE TO THE ORIGINAL IS DEFINITELY INTENTIONAL!
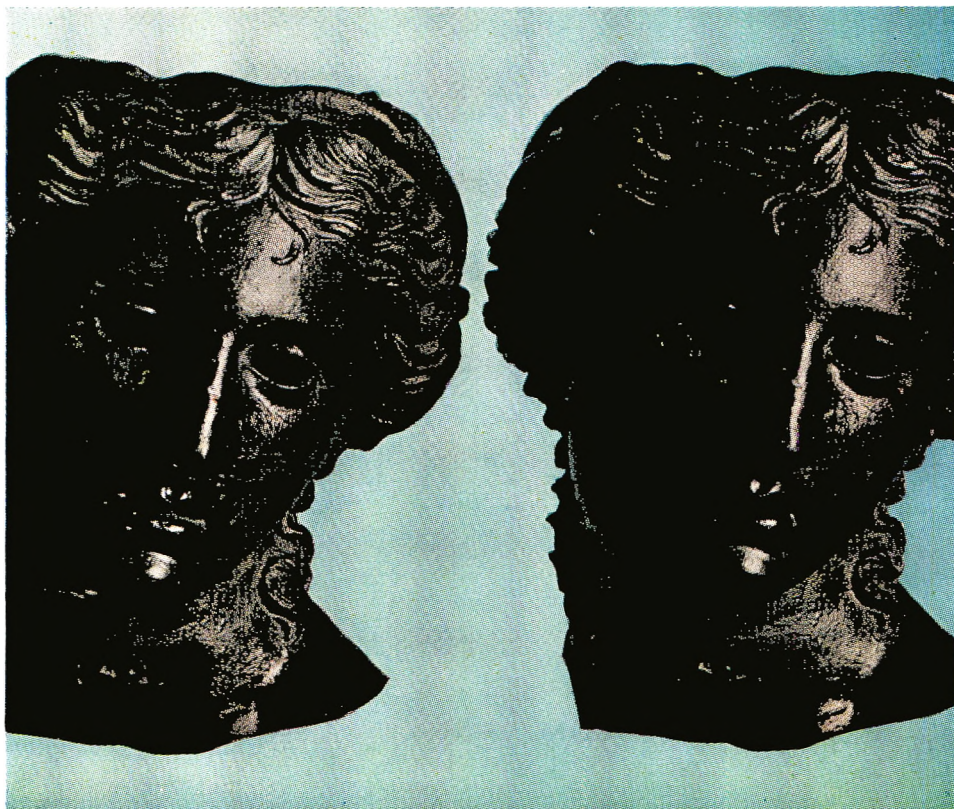
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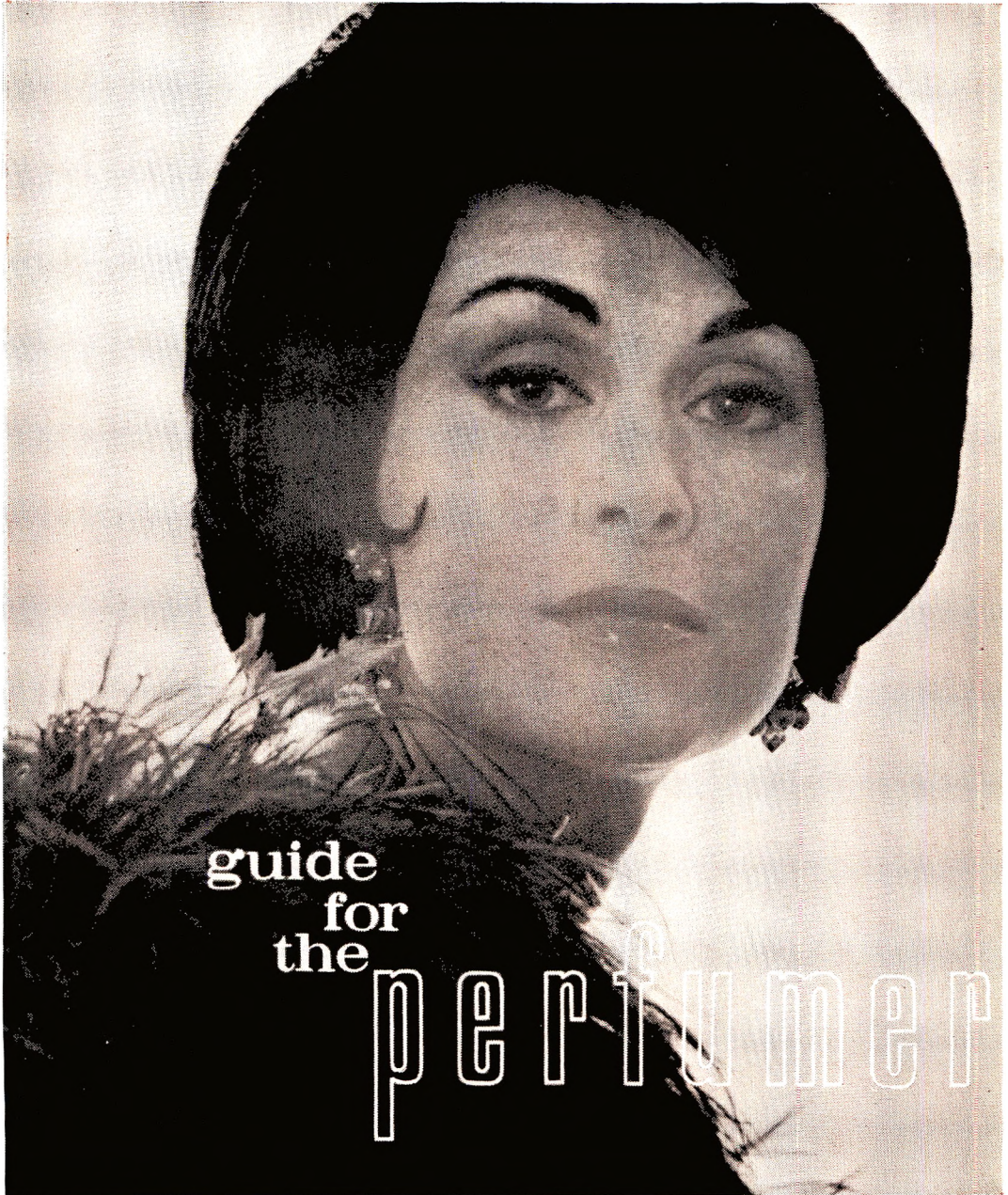
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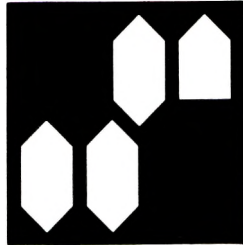
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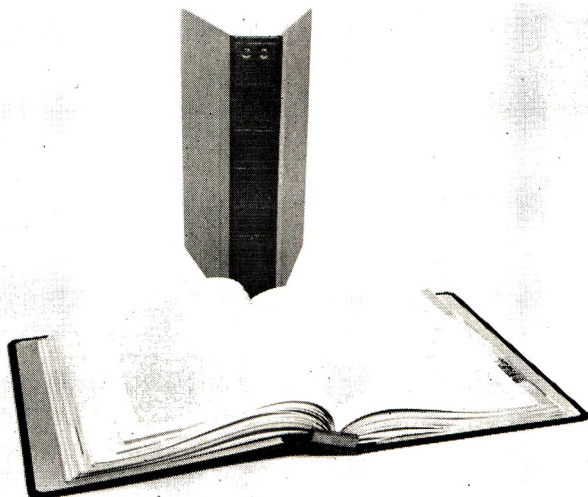
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SYNOPSES FOR CARD INDEXES

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

The hormonal background of the skin: E. C. DODDS.
Journal of the Society of Cosmetic Chemists **16** 431-446 (1965)

Synopsis—The dependence of the skin on the whole of the hormone-producing systems of the body is shown by reviewing the chief actions of the endocrine glands in health and disease. Synthetic compounds with hormonal activity similar to those of the oestrogenic and adrenal anti-inflammatory steroids are mentioned in particular because of their importance as valuable therapeutic aids which have been made available only through the efforts of the synthetic organic chemist. The relation which exists between hair growth and hormones produced by the adrenal glands, ovaries and testes is discussed in detail, and attention is drawn to a recent paper which suggests that application of an ointment containing 1% testosterone propionate might be capable of restoring hair growth in cases of baldness.

Hydrolysis of wax-esters in emulsions: C. A. ANDERSON and E. V. TRUTER.
Journal of the Society of Cosmetic Chemsists **16** 447-463 (1965)

Synopsis—Determination of the interfacial tensions of benzene solutions of wax-esters against aqueous solutions reveals that the esters are not surface active. Moreover, ester/alcohol complexes are not formed at the interface. The experimental evidence suggests that the hydroxyl ion is adsorbed at the oil/water interface. The relevance of the interfacial measurements to the hydrolysis of wax-esters, and the hydrolytic mechanisms in o/w and w/o emulsions are discussed.

An approach to emulsion formulation: B. W. BURT.
Journal of the Society of Cosmetic Chemists **16** 465-477 (1965)

Synopsis—Two series of experiments dealing with heterogeneous systems are reported ; the first concerns mixtures of cresols, soap and water and emphasizes the importance of phase identification. Original work with o-, m- and pcresols is reported. The second series concerns the stability of emulsions of oil, water and a pair of nonionic emulgents ; the results tend to confirm the usefulness of the HLB concept.

The paper concludes with a discussion of the place of phase equilibria in the formulation and theory of emulsions.

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The Hormonal Background of the Skin

The 1965 Medal Lecture by PROFESSOR SIR EDWARD CHARLES DODDS, Bt., M.V.O., F.R.S., The Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London, delivered before the Society of Cosmetic Chemists of Great Britain on 14th April 1965, with Alfred Herzka, President of the Society, in the Chair.

THE CHAIRMAN: Last year the Council of the Society 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.

When considering possible names for the first lecture we were fully aware of the responsibility which lay upon us because the first lecture must inevitably set a precedent for those that follow in future years.   The choice of the Council fell on Sir Edward Charles Dodds and we do indeed consider ourselves very honoured that he has agreed to deliver this first lecture. Sir Charles is, as you no doubt know, Professor of Biochemistry in the University of London and if I were to enumerate his activities and the honours and degrees that have been bestowed upon him I fear there would be no time at all tonight for any lecture.   I therefore wish to limit myself to just a little story.   When I met Sir Charles in order to discus this lecture he stressed his great responsibility towards an audience which would voluntarily come to listen, as opposed to university students who have no option where lectures are concerned. This clearly illustrates Sir Charles, the man.

The following lecture, which was illustrated with lantern slides, was then delivered.

Synopsis—The dependence of the skin on the whole of the hormone-producing systems of the body is shown by reviewing the chief actions of the endocrine glands in health and disease. Synthetic compounds with hormonal activity similar to those of the oestrogenic and adrenal anti-inflammatory steroids are mentioned in particular because of their importance as valuable therapeutic aids which have been made available only through the efforts of the synthetic organic chemist.   The relation which exists between hair growth and hormones produced by the adrenal glands, ovaries and testes is discussed in detail, and attention is drawn to a recent paper which suggests that application of an ointment containing 1% testosterone propionate might be capable of restoring hair growth in cases of baldness.

I must thank you, Mr. President, and your Council for inviting me to give the first of these lectures.   I also feel a certain amount of embarrassment at being presented with the Silver Medal by a Society to which I fear I have made no practical contributions.   You kindly allowed me to choose

the title of my lecture and I, rather naturally, selected the field in which I have spent the greater part of my life's scientific work, namely the study of hormones. I shall attempt in the time at my disposal to indicate to you the potentialities of applying some of the principles of endocrinology to a consideration of the skin and I hope that I shall be fortunate enough to interest yourself and your colleagues in the possibilities of applying endocrinological knowledge to the science of cosmetics.

I understand that the majority of the members of your Society have mainly a chemical or physico-chemical background and, therefore, it will probably not be out of place if I devote a considerable part of the time at my disposal to giving you a brief picture of the endocrine system of the human body. To undertake this in what amounts to a few minutes, is of course a difficult, if not impossible, task, but I hope that this brief account will be a useful background to what we are going to consider later.

In the animal body there are a series of glandular organs secreting fluids which are collected in tubes, or ducts, as they are called, and are emptied into the digestive or urinary tract. As examples of these glands one can quote the salivary glands, the pancreas and, in the case of the urinary system, the kidneys. Anatomists over the centuries became puzzled by the number of other gland-like organs in the body, very similar in structure to the glands with ducts, but differing from them in that the anatomists could find no evidence of a duct or tube. These became known as the "ductless glands," and they include the thyroid, the pituitary, the suprarenals and the gonads. The functions of these ductless glands were not understood until the turn of the century when the concept of internal secretions gradually evolved. It was proved that a gland, such as the thyroid, produced a secretion which went directly into the blood stream. Later, in the early part of the present century, this internal secretion was called a hormone. From then onwards to the present day a vast amount of research work has been done on the nature of these hormones and their mode of action. Time does not permit us to go into this matter in great detail, but I should like to describe very briefly the chemical nature and functions of the more important of these internal secretions or hormones. The most important internally secreting gland in the body is the pituitary which is situated at the base of the brain and carefully protected by a bony cage at the base of the skull. The pituitary consists of two parts, the anterior lobe and the posterior lobe. The anterior lobe secretes a whole series of hormones which act upon all the other internally secreting glands. These are known as trophic hormones and from the

chemical point of view they are proteins. The most important are the gonadotrophic hormones which react on the sexual organs, namely the testes in the male and the ovaries in the female, and are responsible for their activation and, in turn, for their secretion of hormones which control the secondary sexual characteristics with which we shall be dealing shortly.

Another pituitary trophic hormone is the thyrotrophic hormone which again is responsible for the thyroid gland making it, in turn, secrete its hormone thyroxine. Then there is the adrenocorticotrophic hormone or ACTH, as it is called, which is responsible for stimulating the suprarenals to produce their hormones. All of these as we shall see later, have a bearing on the skin.

The posterior lobe produces peptide types of hormones which affect plain muscle, renal secretion and blood pressure. In so far as we know, these have no connection whatsoever with the functions of the skin. We can see, therefore, that the anterior lobe of the pituitary can be regarded as the master gland of the endocrine system, or as it has aptly been described "the conductor of the endocrine orchestra."

Let us take a very quick look at the chemistry and functions of the hormones secreted by those glands controlled by the pituitary. Firstly the thyroid. Its hormone is the only iodine-containing internal secretion and is known as thyroxine for which the formula is shown in *Fig. 1*. This

$$HO - \overset{I}{\underset{I}{\bigcirc}} - O - \overset{I}{\underset{I}{\bigcirc}} CH_2CH.NH_2COOH$$
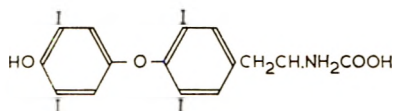
THYROXINE

Figure 1

is a crystalline chemical substance that can be synthesized with relative ease and when administered to a thyroidectomized animal or person it will replace the functions of the missing gland. It is a stimulator of metabolism and raises the energy exchange of the tissues in the body, including the skin. There is a well known disease associated with atrophy or degeneration of the thyroid gland. This is known as myxoedema and it is characterized by a thickening and coarsening of the skin. The administration of thyroxine to such a patient results in a cure of the myxoedema with a return of the skin to its normal condition. So, we have here the first example of an endocrine influence on the skin. Adequate secretion of the thyroid hormone is necessary for the maintenance of normal skin. Administration of excess of thyroxine produces a stimulation of metabolism

with increased oxidation in the body.   A similar condition occurs in the disease known as Graves' disease, or exophthalmic goitre.   Here the skin becomes thin, and paper-like in contrast to the thickening of myxoedema.

It is well known that disturbances of the sex glands produce changes in the skin.   Let us consider first of all the hormones produced by the ovaries.   These belong to the well known group of steroidal substances, and *Fig. 2* shows the three principal hormones produced in the female

OESTRONE

OESTRADIOL   OESTRIOL
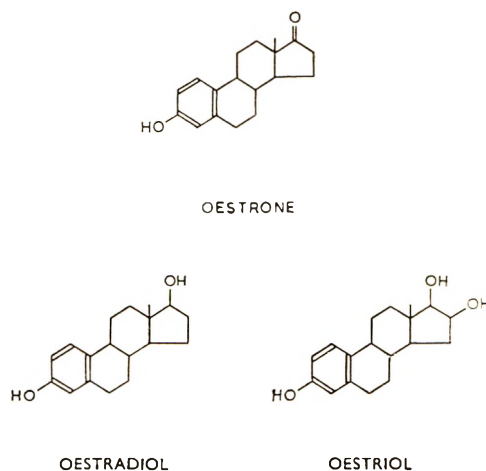
Figure 2

body.   These are oestrone, oestriol and oestradiol.   If the ovaries are removed or the menopause occurs, when their function ceases, it is well known that coarsening and thickening of the skin occurs, rather similar, but not so marked, as that in myxoedema.   We shall see later that these substances have been the subject of considerable experimentation in the cosmetic world.   Before leaving them, one might also mention the purely synthetic analogue that was produced by myself and my colleagues in 1938 (1), namely stilboestrol, the structure of which is shown in *Fig. 3*. This substance possesses all the properties of the naturally occurring hormone and it has also been the subject of experimentation in the cosmetic industry.

The secretion of the testes, the male hormone, is also a steroidal sub-stance known as testosterone, and is shown in *Fig. 4*.   We shall be referring to extensive experiments conducted with the use of this material at a later stage of this discussion.

STILBOESTROL
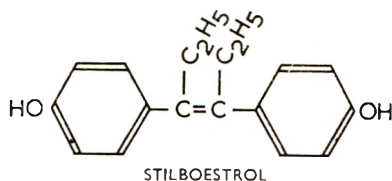
Figure 3

Some of the most interesting hormones have been isolated from the suprarenal gland. These again are steroidal bodies. If the suprarenal glands of animals or man are removed, death invariably takes place. In the human subject destruction of the suprarenal gland occurs in the pathological process known as Addison's disease. This condition is characterized by a number of clinical manifestations, but from our point of view the most interesting are the characteristic and diagnostic changes that occur in the skin. Addison's disease is attended with marked pigmentation of the skin. This is of a brownish character and occurs particularly at the bends of the limbs and where there are skin creases.

TESTOSTERONE
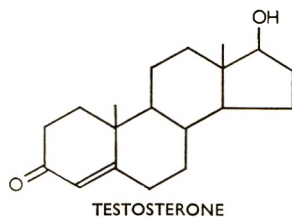
Figure 4

The pigmentation also spreads to the mucous membranes and can be seen clearly in the mouth. A whole series of substances are produced by the adrenal cortex and *Fig. 5* shows the structure of some of them which are of interest to us in the context of this lecture. They are characterized by having the well known cyclopentenophenanthrene nucleus and either a ketone or a hydroxyl group in the 11-position. For many years these substances were academic curiosities, being isolated from natural sources in mg quantities. Addison's disease was successfully treated from the 1930's onwards by the use of an extract of suprarenal glands obtained from the slaughter house, but no practical interest was shown in the pure adrenocortical steroids until the work of Hench (2,3) showed that one of these substances, namely cortisone, possessed very valuable antirheumatic properties. The demand for cortisone for the

CORTICOSTERONE HYDROCORTISONE

DEHYDROCORTICOSTERONE CORTISONE
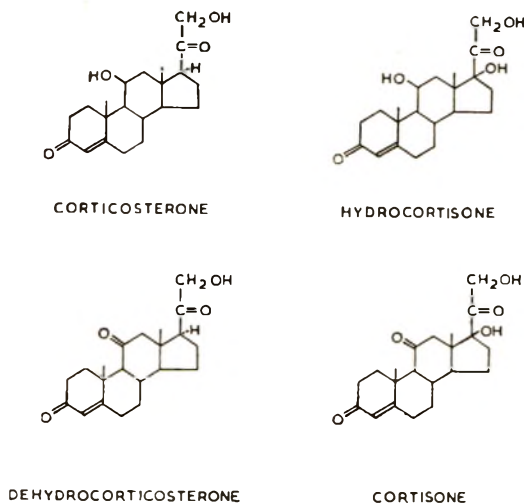
Figure 5

treatment of rheumatoid arthritis resulted in an intense concentration of research, and the synthetic production of cortisone and cortisone-like substances. As is well known, the synthesis was conducted by starting with natural steroids such as the bile acids and then effecting a chemical rearrangement of the molecule so that cortisone and similar substances were produced. These compounds have a profound influence on diseases associated with disturbances of collagen metabolism. Rheumatoid arthritis belongs to this group of diseases known as the collagen group which also includes conditions such as systemic lupus erythematosis and scleroderma. In this condition characteristic lesions of the skin appear of which the most distressing is the very disfiguring alteration in the face with a thickening and blotching of the skin over the nose and cheeks giving an unfortunate appearance which has been likened to a butterfly, the nose being the body and the cheeks the wings. The administration of cortisone will frequently cause this condition to disappear. This has led to intensive experimentation with substances of this type on the skin. Before leaving this group I would like to refer to one of them, namely aldosterone, which was discovered by Tait and Simpson working in our hospital. This has a characteristic chemical structure, determined during collaboration with chemists in Basel (4), with an interesting oxygen bridge which is seen in *Fig. 6*. This substance, very briefly affects the electrolyte balance of the body and its administration causes retention of sodium. Great attention has been paid to the effect of electrolyte balance on the skin and it may
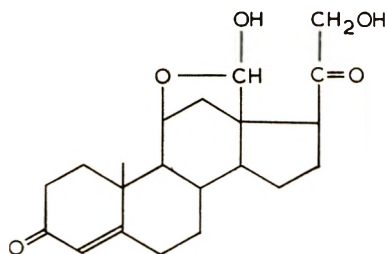
ALDOSTERONE

Figure 6

well be that future research will show that aldosterone plays a part in the
regulation of the normal function of the skin.   Before discussing the effects
of topical application of hormones to the skin, I would like to clarify the
question of the possible cancer-producing potentialities of such applications.
A great deal of sensational and inaccurate statements have been expressed
on this subject.   It has often been suggested that the addition of oestrogens,
such as oestradiol and stilboestrol to face creams constitutes an actual risk
of the development of cancer in the users.   It has also been stated that
oestrogens are cancer producers.   This, like so many statements, is a
partial truth, and like so many others, when taken from their scientific
context, can be completely misleading.   Let us just look at the facts:
It was shown many years ago by Professor Lacassagne (5) that if one
injected oestrone into very young mice and continued to inject them for
the rest of their lives, a very high proportion of the animals in later adult
life developed cancer of the breast.   Very careful work of a genetic
character over a number of years after Lacassagne's observation showed
that oestrone and other oestrogens would only produce an increase in the
incidence of carcinoma of the breast in animals that had the genetic
possibility of developing carcinoma of the breast.   It is possible to produce
strains of mice which, no matter how long they live, will never produce
carcinoma of the breast and administration of oestrogens to these animals
will not produce this condition.   From this point of view one can state
that oestrogens are able to stimulate but not initiate the production of
cancers.   The fear that the topical application of oestrogens will produce
cancer is a confusion with what are known as carcinogenic hydrocarbons.
In the middle of the 18th century a distinguished surgeon at St. Bartholo-
mew's Hospital, Mr. Percival Pott, demonstrated conclusively that cancer
of the skin of the genitalia of chimney sweeps was due to prolonged exposure
to soot.   It will be remembered that in those days no one bathed at all,

and that contamination with soot would possibly last a lifetime.   It was
not until the 1920's that the chemical nature of the cancer-producing
agent in soot and tars was identified.   This was done by the late Sir Ernest
Kennaway, Sir James Cook and their colleagues at the Royal Marsden
research department, now known as the Chester Beatty Institute (6–9).
They showed that the cancer-producing substances were condensed carbon
ring compounds of the type of dibenzanthracene and benzpyrene which
are shown in *Fig. 7*.   These substances, if painted on the skin of mice
over long periods, will produce cancer.   On the other hand, painting of

DIBENZANTHRACENE   BENZPYRENE

Figure 7

the skin of mice with oestrogens under the same conditions will never
produce cancer of the skin and, therefore, we can with safety say that
there is no risk of cancer being produced in the human skin by the
application of cosmetics containing oestrogens.

We have now reviewed the endocrine system of the human body and
we can see the types of chemical compounds that the body produces in
order to regulate growth, development and metabolism.   With only one
exception, I have described naturally occurring products but I did mention
the hormone analogue stilboestrol which has all the biological properties
of the naturally occurring oestrogens.   It is, I think, essential at this stage
to draw your attention to another group of chemically modified hormones,
namely the substituted corticosteroids.   I have already shown you the
formulae of some of the naturally occurring substances such as cortico-
sterone and cortisone.   Very powerful new substances have been developed
by organic chemists using these molecules as a basis and introducing new
groups.   The most successful of these series are the fluorinated compounds
of which the most important are *fluocinolone, triamcinolone* and *fluran-
drenolone* which are shown in *Fig. 8*.   One of the most widely used has
been βmethasone 17-valerate, the properties of which were reviewed
recently by Williams *et al* (10).   It has been shown that these substances
penetrate the skin when applied in ordinary media, but if they are applied

TRIAMCINOLONE

BETAMETHASONE 17-VALERATE

FLURANDRENOLONE

FLUOCINOLONE
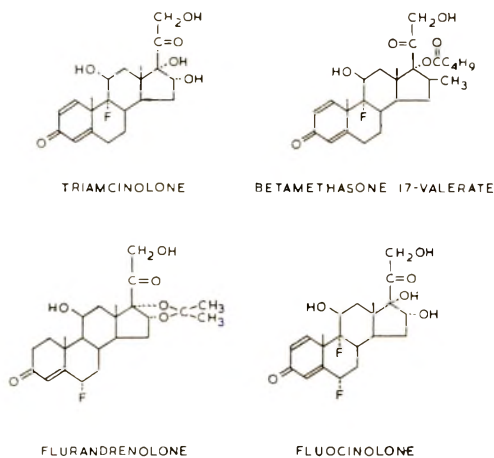
Figure 8

with what is known as the occlusion process, that is to say under a sealed cellular cover, then high concentrations of these substances occur in the skin and produce very profound effects. It is no exaggeration to say that the whole of dermatology is today undergoing a revolution as the result of these experiments. Apparently one of the primary actions of these fluorinated compounds is that of the well known anti-inflammatory action of the corticosteroids. Workers in the Glaxo Laboratories have developed a special test (11) and it has shown that the anti-inflammatory activity bears a relationship to the vaso-constrictor activity of the compounds. This is a highly specialized subject and I have really no time to go into the details, but there can be no doubt that by the application of the new compounds many skin diseases, such as psoriasis, which are at present regarded as incurable, will be amenable to treatment.

Before leaving the hormones generally, I would like to say a word about the level at which they act. As you will doubtless be familiar, the world of the biologist, and in fact of the pathologist and the medical consultant, is moving to the sphere of molecular biology and it, therefore, requires speculation as to whether the substances that I have listed require the whole body to produce their reactions or whether they can act locally, let us say, for example, on certain layers in the skin. There is no doubt that the substances that we have enumerated act in two ways, some on organs and others on specific cellular elements of the tissues.

On the other hand we know that the addition of thyroxine to suitable tissue fractions will result in an increased oxidation. We also know that

some of the hormones, such as testosterone and the oestrogens, act on certain parts of the reproductive organs and also on the integument.

Having assembled all this information it is rather difficult to know how to proceed in a purely logical manner. I do not propose to plunge into the complications of dermatology as the pathological signs of this subject are so obscure and many of the conditions rare, that I think it extremely unlikely that at this stage of development we could gain anything really definite from the point of view of the cosmetic chemist. Really very little is known about the aetiology or the treatment of the commoner skin diseases other than those due to infection and parasitism. We are beginning to understand a great deal more about allergic conditions but I think that this aspect cannot be included in this lecture.

Let us consider first of all the evidence and value or otherwise of the addition of hormones to cosmetic preparations for local application. I well remember in the early 1930's, when Schering-Kahlbaum A.G. in Berlin, succeeded in producing oestradiol in a crystalline stabilized form for the first time. I also remember the very great hopes that were held out for this material, which of course immediately assumed an importance in gynaecological therapy and became the standard treatment for the symptoms of the menopause. Extensive experiments were conducted in the U.S.A. and were, I think, reported by the Council in Pharmacy of the American Medical Association. The results of adding oestrogens to cosmetic preparations were disappointing, to say the least of it. Contra-indication was very quickly observed in that if the concentration was to be effective enough material was absorbed to interfere with the regular menstrual cycle. Looking back on these experiments with the knowledge that we have gained during the past 30 years, it is not surprising to me that the results were inconclusive, in fact with the knowledge that we have of the necessity for blind and double blind tests for relatively crude things like pain, etc., one wonders if it will ever be possible to check up finer variations in the treatment with reinforced creams. This subject has been looked into very carefully by Ebling (12) who has concluded that the hormone creams are no better than those without hormone additives.

I would like to make some reference now to the use of testosterone in creams, but this will take me very briefly to the subject of hair growth on the skin. This again is a vast subject of which it is not possible here to make more than passing reference.

Hair Growth

The integumentary appendages have repeatedly been shown to be target organs for sex hormones, and this is seen most strikingly in birds which instead of having hair grow feathers, in many cases of vivid colour, from the dermal layer. The sex of the bird in many species determines whether the plumage is drab or colourful, and often whether the feathers are long and sweeping and suitable for decorating ladies' hats, and the hormonal effects have been described at length by Domm (13). Surgical removal of the ovaries from a hen bird will induce the development of male plumage and reversion to the female type is possible by subsequent injections of female hormones. It is even possible to see this reversal during the development of a single feather so that the tip may be characteristic of one sex and the proximal portion of the other sex.

Similarly, the mammals have differences between the sexes in hair growth; thus in rats, hair length in the female is shorter than in the male, and this has been shown to be due to different rates of growth, as also is the case with the axillary hair in man.

Two chief phases, growing and resting, are seen in the development of every hair. During the growing phase a group of the dermal cells become active and produce a papilla which grows down into the subdermal tissues. This finger of dermal cells cannulates and from its base arises the hair shaft protected at first by a sheath. This shaft is composed entirely of keratinized dead cells and its length is governed by the duration of the growing phase when the follicle is active, and by the rate at which the dying and keratinization of the cells of the basal papilla proceeds. The resting phase begins when the activity of the hair follicle ceases and lasts until the "club" hair, as it is called, is shed.

Regional differences in the length of hair over the body are chiefly due to differences in the duration of the growing phase, and regional differences in the rate of growth are usually small. Thus, the hairs of the eyebrows have a short growing phase and a long resting period, while the scalp hairs have a very long growing period and a short resting period.

In some animals hairs develop in waves of follicular activity over the surface of the body, but in man the follicles are non-synchronous and all stages of development lie together over the body.

It is possible to predict that hormones which may be able to affect hair growth will only be able to act at certain times during the development and these are by:

1. Induction or inhibition of the growing period.
2. Affecting rate of growth during the growing period.
3. Limiting or lengthening the growing period.
4. Promoting or inhibiting the shedding of "club" hairs.

We will first consider the influence of the adrenals on hair growth with these phases in mind, particularly the first, for it is at this point that any measures aimed at curing alopecia or baldness must be directed.

Since clinically, hirsutism is often associated with adrenal tumours it might be expected that a relationship exists between hair growth and adrenal hormones, but the sum of experimental evidence would seem to suggest the opposite.

Adrenalectomy has been shown to be followed by earlier hair growth in the rat and had a hardly noticeable effect on the loss of "club" hairs. On the other hand, there was retarded growth of hair in rats with hypertrophied adrenals induced by restriction of their diet. This experiment has introduced a complicating dietary factor and no effect on hair growth was seen when ACTH was used to induce hyperadrenalism. It is only since 1950 that administration of adrenal hormones have been studied for their effects on hair growth by Johnson (14) and Whiteley (15). They have shown, in rats, that cortisone administered systematically and hydrocortisone topically inhibit the initiation of the growing period. Following cortisone, growth did not recommence until 13 to 20 days after cessation of the treatment.

It has been suggested that cortisone might inhibit regrowth of hair and follicular activity by adversely affecting the blood supply to the follicles.

The experimental evidence would suggest that the adrenal hormones might be more effective depilatory agents than hair restorers though Dillaha and Rothman (16) have reported some success in treatment of alopecia with cortisone in 1952, and some cosmetic preparations purport to contain hydrocortisone derivatives.

The sex hormones would appear to play a very definite part in regulating hair growth as the following observations in man suggest. The adrenal hormones proved disappointing after the original premise relating hirsutism with adrenal activity suggested that they had possibilities which might be exploited. The fact is that hirsutism in adrenal hyperactivity is not due to the glucocorticoids secreted by the adrenals, but to the androgenic steroids which are also increased in these cases. In women hair loss offers a complicated picture because of the demands of social habit and fashion which require the application of chemical, thermal and mechanical injuries

to the hair. However, it is certain that during pregnancy the growing phase of hair development is lengthened and the resting phase is delayed. The longer hair grown during pregnancy is shed during the puerperium sometimes giving a condition known as post-partum alopecia, followed by normal hair growth.

In experimental studies with rats it has been shown that hair growth is inhibited by injection of oestrogenic substances in amounts which are inimical to body growth, and by application of them to the skin. Later studies, also in rats, demonstrated that injections of oestradiol delay the start of the growing phase and decrease the rate of growth, but that loss of the club hairs is inhibited, consequently increasing the length of the resting phase.

Androgens, on the other hand appear to stimulate the hair follicle directly giving rise to hirsutism, but many experiments have not shown them to be effective as hair restoratives in baldness, though they are able to offset the effects of large doses of oestrogens which cause loss of hair. Unlike the oestrogens, androgens were found to have no effect on the growth rate of the hair, or on the loss of "club" hairs.

The increased hair length met with in pregnancy would seem to suggest that progesterone could influence hair growth, but I have not heard that women taking the progestational contraceptive pill suffer from an increased amount of hair.

Before leaving the sex steroids it is necessary to mention the inter-relationship of these hormones with those of the adrenals in their effect on hair growth. In the rat the adrenal hormones enhance the effect of oestradiol in delaying the start of the growing phase, but there seems to be no synergism or antagonism by androgens since adrenalectomy of male rats had no effect on hair growth. The adrenals do not seem to be important either in relation to the loss of club hairs in the male or the female rat.

The thyroid gland is the source of other hormones which might be of interest in this connection. In cases of myxoedema there is loss of thyroid function which is often associated with loss of hair, while in goitre or hyperthyroidism hirsutism is often seen. The thyroid has also been shown to be involved in hair growth in animal experiments. However, when triiodothyronine is given to normal subjects the androgen/corticoid ratio of the excreted steroids has been shown to be altered towards excess of the androgens and this might be the actual mediator between the thyroid and hair growth. Berman (17) on the other hand applied thyroxine

topically to the skins of dairy cattle which undergo an annual cycle between growing and shedding, and colour of hair. The long, full, woolly winter coat is gradually replaced by thicker, shorter, more reflective summer hair. He found that the thyroxine treatment affected rate of growth and increased pigmentation at a level of only $6\mu g/cm^2/day$ which seems to be insufficient to affect androgen secretion. It is not known whether thyroxine has any regenerating effect on hair follicles.

To the intense surprise of the experts an article appeared recently (18) on the effect of the topical application of testosterone on the growth of hair in baldheaded people. So impressed were the Editorial department of the particular journal that they had an Editorial entitled "Baldness breakthrough" (19). As we are obviously going to hear a lot more about this I thought it advisable to discuss it in some detail. The loss of hair in the middle-aged and elderly male has been a subject of comment from time immemorial. The fact that the condition is practically confined to the male indicates that there may possibly be some endocrine background. Various other explanations have been put forward such as size, thickness of the scalp and so forth and inferior blood supply, but I think I am right in saying that there is no commonly agreed explanation for this condition. Again, I well remember when the Germans produced for the first time, in relatively unlimited quantities, pure crystalline testosterone. Extensive experiments were conducted using the material both by injection and by local application, but the results were uniformly negative. It is, therefore, surprising to turn to the paper by Papa and Kligman (18) referred to in the Editorial. The authors review the aetiology and then proceed to a description of their experiments. The experiments were conducted on prisoners who were chosen for their complete frontocentral denudation. Fortyone prisoners were selected, aged from 29–78 yr and the duration of the baldness from 1–30 yr. Twentyone of the subjects were selected for test and each were treated with 0.5 g of a 1% testosterone propionate ointment in a hydrophilic base. This material was applied once a day to the scalp. The remaining 30 controls were treated with the vehicle alone. I think it best is to quote the authors' actual words of the results:—

"In this preliminary study, no effort was made to quantitate the amount of regrowth of hair. A positive response to testosterone propionate ointment was the unmistakable appearance of longer, stouter, terminal type hairs in an area which previously contained nothing but nearly invisible lanugo-type hairs. By this criterion 16 of the 21 androgen-treated

subjects showed indisputable hair growth. None of the control group treated with hydrophilic ointment showed this change. We judged that perhaps 10% to 15% of the original follicular population was stimulated. The pattern of regrowth progressed in the reversed order of loss; greater response was noted about the parietal and occipital area. These peripheral areas, adjacent to surviving terminal hairs, reacted earliest and best. Evidently the most recently and incompletely involuted follicles are capable of optimal response.

"The age of the subject, whether young or old, did not appear to affect the probability of stimulation. Surprisingly, we have the tentative impression that the result was not clearly dependent on the duration of baldness. A return of pigmentation in white-haired individuals was not observed. Although the regrowing hairs were terminal and coarser, they probably did not reach the length and thickness of which the follicle was originally capable. In no instance was there a restoration of a thick, luxuriant pelage which wiped out the impression of baldness.

"Within the short period of this study no individual was adversely affected by the treatment. There was no evidence of salt retention, prostatic hypertrophy, or return of axillary or pubic hair in older individuals. Although difficult to document, the three most elderly subjects experienced improvement on mood, vigour, and appetite, which impressed the attending personnel as well as the subjects, perhaps reflecting the anabolic activity of testosterone."

Admittedly the photographs do not look particularly impressive, but of course the really important point is that the authors have shown that the balding process is a reversible one. If this progress can be maintained then it is highly possible that more active compounds will be found.

In conclusion one can, I think, say that the greatest difficulty in preparing this lecture has been in the selection of the material. Your President invited me to give this lecture very nearly a year ago and I commenced work at once. I very quickly realized that I was preparing a course of lectures not just one. It is perhaps unwise to prophesy what will happen. My own feeling is that little progress can be expected out of the addition of the standard hormones to cosmetic preparations. I think that we have had sufficient experience during the last 30 years to indicate to us that there is unlikely to be any great advance with the original preparations. I do feel, however, that with these new highly active corticoid preparations and their effect on pathological conditions of the skin, it may be that a

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new era is about to be introduced and that the cosmetic chemist should certainly keep his eye very firmly glued to this field in which rapid advances are being made from day to day.

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The Chairman then presented the lecturer with the Society's silver medal, amidst applause from the audience.

MR. R. CLARK: It is my pleasure this evening to thank you formally for having delivered our first Medal Lecture. Less formally, as one of your obviously interested audience this evening, I would like to thank you for the very clear and concise picture of what is a fairly complex subject. Among your audience here tonight there are a number who already knew a considerable amount about this subject and there are many, of course, like myself who only have a superficial knowledge of it. However, irrespective of our previous state of knowledge, I am sure that all of us here tonight now have a much clearer understanding of the role played by endocrinology in that mixture of scientific discipline which we choose to call cosmetic science. First occasions are always somewhat special, and indeed you have made this a special evening for us tonight. Thank you, Sir Charles.

The Society's Silver Medal (full size)

Sir Charles Dodds delivering the 1965 Medal Lecture

Hydrolysis of Wax-Esters in Emulsions

C. A. ANDERSON† and E. V. TRUTER*

Synopsis—Determination of the interfacial tensions of benzene solutions of wax-esters against aqueous solutions reveals that the esters are not surface active. Moreover, ester/alcohol complexes are not formed at the interface. The experimental evidence suggests that the hydroxyl ion is adsorbed at the oil/water interface. The relevance of the interfacial measurements to the hydrolysis of wax-esters, and the hydrolytic mechanisms in o/w and w/o emulsions are discussed.

INTRODUCTION

Before an ester formed from a water-insoluble acid and a water-insoluble alcohol, i.e., a wax ester, can be hydrolysed in an emulsion, two conditions must be fulfilled. Firstly, the reactants must be able to penetrate the interface, and secondly, the reactants in the interface must be suitably oriented.

From measurements of the surface potential and the rates of hydrolysis at the air/water interface (1,2) it has been deduced that esters of the type under consideration, even at relatively low surface pressures, are folded into a V-shape, the ester linkage being in the interface. A major difficulty in interpreting the mechanism of emulsion hydrolysis of esters in these terms is that even short-chain esters are very weakly surface-active, so that the reaction should not reach completion because the reactants are gradually displaced from the interface by the more surface-active products of the hydrolysis. In o/w emulsions the reaction does, in fact, come to a halt before all the ester has been hydrolysed. In unexpected contrast, w/o

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†Present address : Wool Research Laboratory, P.O. Box 21, Belmont, Geelong, Australia.
*Textile Chemistry Laboratory, The University, Leeds, 2.

emulsion hydrolyses proceed to completion. In an attempt to explain these observations, it was postulated (3) that the surface-active species was an association complex of an alcohol and an ester, a suggestion which was in accord with the known behaviour of mixtures of wax-alcohols and their esters as w/o emulsifying agents. Thus, although the emulsifying powers of wax-esters are negligible, the emulsifying power of a wax-alcohol plus one of its esters is usually greater than that of the alcohol alone, the difference increasing as the molecular weight of the acyl radical of the ester increases (4,5). The emulsifying power is here defined as the percentage of water that can be emulsified by a sample of liquid paraffin containing 5% of the surface-active agent. For cholesteryl esters, the following values have been recorded (5) :—

2.5% cholesterol	120
5.0% cholesterol	240
2.5% cholesterol + 2.5% cholesteryl acetate	410
2.5% cholesterol + 2.5% cholesteryl butyrate	620
2.5% cholesterol + 2.5% cholesteryl palmitate	1180

We have investigated the nature of the interaction between cholesterol and cholesteryl stearate and between $n$hexadecanol and $n$hexadecyl palmitate, and find that they do not associate in the interface. Moreover, the ester itself is devoid of surface activity. Hence, in w/o emulsions which proceed to completion, one of the ionic reactants must be adsorbed at the interface.

EXPERIMENTAL

Method

Measurements of the interfacial tensions were made by the drop-weight technique (6), using a micrometer syringe (7) fitted with a stainless steel capillary tube. Calculations are based on the relation :—

$$\gamma = \frac{\mu(\varrho_1 - \varrho_2)g\beta}{r}$$

where
γ is the interfacial tension (dynes/cm),
μ is the volume of the drop at the moment of detachment (cm³),
ϱ_1 and ϱ_2 are the densities of the two bulk phases (g/cc),
β is the correction factor of Harkins and Brown (6), and
r is the detachment radius (cm).

This technique is very suitable for investigating ageing effects, and is accurate provided that the detachment perimeter of the pipette is sharply defined, and accurately known. The micrometer syringe was calibrated at various temperatures, and the densities of the solutions were determined with a Perkins pyknometer at the appropriate temperatures. Normally, the aqueous solution was contained in the pipette, but we ascertained that the results were unaffected by reversal of the positions of the two phases.

Materials

Water was deionized by passing it through a mixed-bed resin *Elgastat* ; its specific conductance was less than 2.5×10^{-7} ohm^{-1}cm^{-1}. It has been shown that some resins give deionized water containing traces of material the surface activity of which can be detected only under acidic conditions (8) ; other products seem satisfactory (9). We compared the surface activities of deionized water, and that obtained by double-distillation from potassium permanganate in a barraglass still and could find no difference between them. *Benzene :* A.R. grade benzene was redistilled from an all glass apparatus ; it had b.p. 80.1°. Whenever new batches of benzene or water were used, the interfacial tension was determined ; the values were invariably reproducible to 0.08 dyne/cm. *Cholesterol* was purified by Fieser's method (10) ; it had m.p. 147.2° and did not absorb in the ultraviolet. *Cholesteryl stearate* was recrystallized seven times from acetone. Before each recrystallization, the solution was treated with activated charcoal, and then filtered through a short column of activated alumina. It had m.p. 78.0–78.8° (to an anisotropic liquid) ; although it had no maximum in the UV absorption spectrum down to 220 nm, at 230 nm the rapidly diminishing value of the extinction coefficient was 0.09 l.g^{-1}cm^{-1}. *Hexadecyl palmitate* was synthesized from pure hexadecanol (m.p. 49.5°) and pure palmitic acid (m.p. 63.1°). After five crystallizations from acetone and two from ethanol, the product had m.p. 52.9°.

OBSERVATIONS

The interfacial tension between benzene and water did not show any ageing effect between 30 sec and 75 min. The values are shown in *Table I*, both deionized water and double-distilled water giving the same values. The value at 20° is slightly lower than that given in the International Critical Tables, viz. 35.0 dynes/cm, and higher than that found by Pilpel (11), namely 34.0 dynes/cm.

Table I   Interfacial tensions of water against benzene

Temperature	γ (dyne/cm)
20°	34.4
40°	32.8
60°	31.1

Interfacial tensions of solutions of cholesterol in benzene against water are shown in *Figs. 1 and 2*, no ageing effects were observed.   Solutions of cholesterol, even when stored in the dark, give progressively lower values
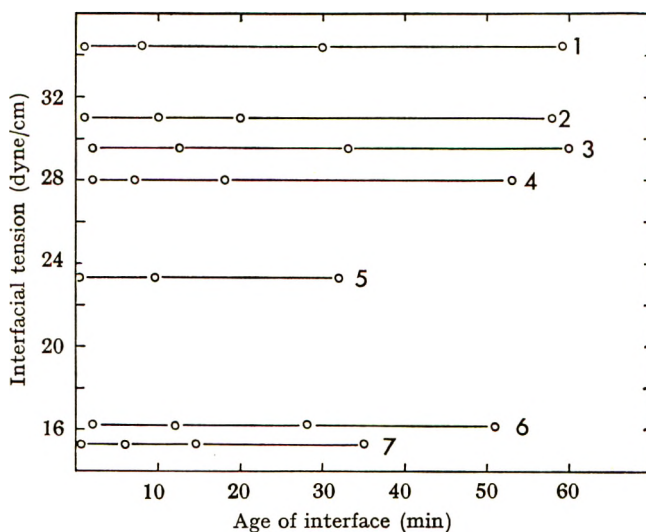
Figure 1

Interfacial tensions of solutions of cholesterol in benzene against water as a function of time.

1.	0.0	mol/l	20°
2.	0.0	mol/l	60°
3.	0.025 mol/l		60°
4.	0.05	mol/l	40°
5.	0.04	mol/l	20°
6.	0.20	mol/l	40°
7.	0.10	mol/l	20°

for the interfacial tension, presumably because of auto-oxidation.   *Fig. 3* shows that the oxidation products of cholesterol affect not only the values of the interfacial tensions, but they may also introduce a marked ageing effect.

Cholesteryl stearate showed a slight ageing effect up to about 25 min, the interfacial tension falling by 1.3 dynes/cm at 20°.   The equilibrium interfacial tensions are shown in *Fig. 4*.   Although the surface activity is
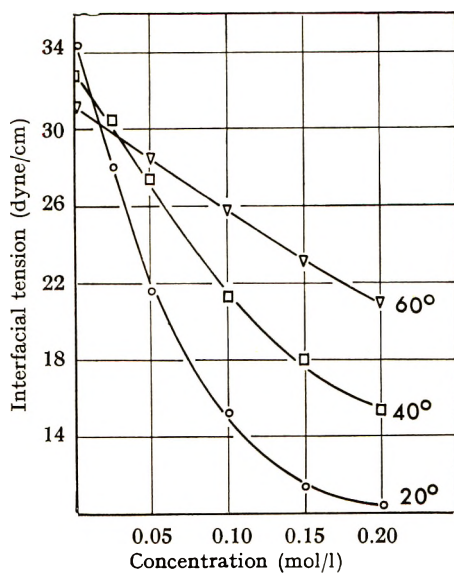
Figure 2 Interfacial tensions of solutions of cholesterol in benzene against water, as a function of concentration.
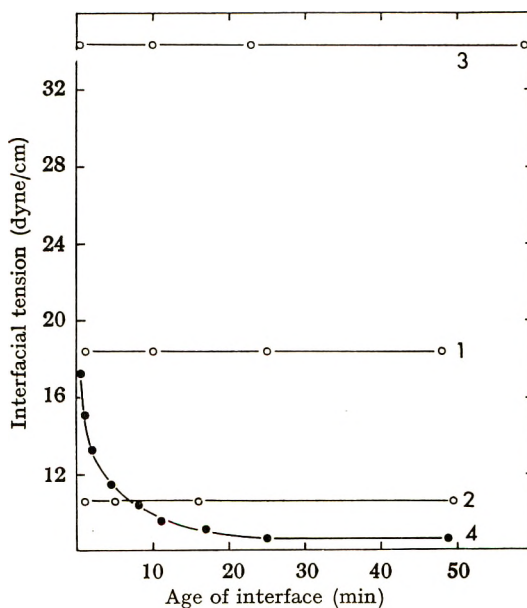
Figure 3 Effect of storage and of irradiation of cholesterol on the interfacial tensions of its solutions in benzene against water ; at 20°.

1. 0.075   mol/l ; fresh solution
2. 0.075   mol/l ; after 90 days' storage
3. 0.0018 mol/l ; fresh solution
4. 0.0018 mol/l ; after irradiation
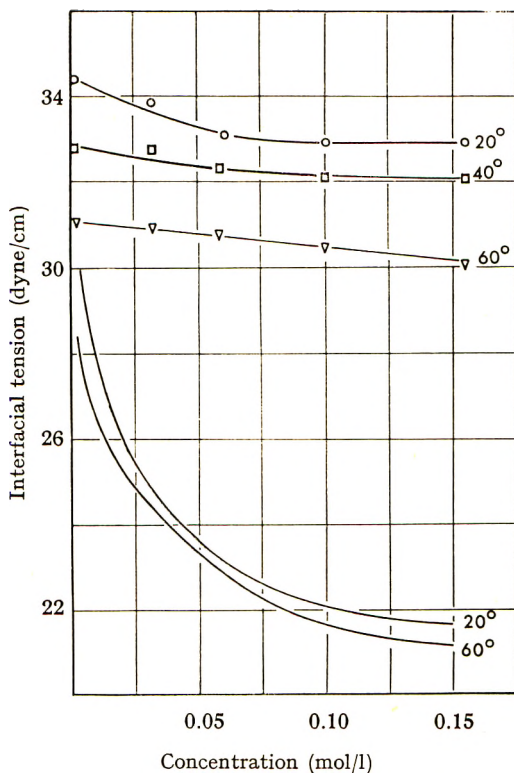
Figure 4   Equilibrium interfacial tensions of water against solutions of cholesteryl stearate in benzene.   Upper set of three curves: for the purest ester.   Lower pair of curves: for ester which had been recrystallized only three times.

slight, it is, nevertheless, higher than that expected.   Similar measurements with solutions of commercial cholesteryl stearate which have been treated with charcoal and recrystallized only three times are also recorded in *Fig. 4*.   It is seen that the less pure ester is markedly surface-active, so that the slight surface activity of our purest sample of ester probably arises from the traces of impurity indicated by the UV spectrum.

The interfacial tensions of systems containing cholesterol and the purest available cholesteryl stearate are shown in *Table II*.   It is seen that the surface activity of the mixture containing both ester and alcohol is not significantly different from that of cholesterol alone.

Table II   Interfacial tensions of solutions of cholesterol plus cholesteryl stearate in benzene against water.

Temperature	Cholesterol (mol/l)	Ester (mol/l)	γ (dyne/cm)	γ (for cholesterol alone at the concn. shown in column 2)
20°	0.0300	0.0100	25.9	26.1
	0.0200	0.0200	29.6	29.4
	0.0100	0.0300	32.7	32.5
40°	0.0300	0.0100	29.6	29.3
	0.0200	0.0200	31.1	30.8
	0.0100	0.0300	31.9	31.7
60°	0.0300	0.0100	29.5	29.6
	0.0200	0.0200	30.0	30.2
	0.0100	0.0300	30.3	30.7

Similar measurements for hexadecanol and hexadecyl palmitate once again showed that the ester was not surface-active, and that it did not exert a synergistic influence on the properties of the alcohol.

Table III   Interfacial tensions of equimolar mixtures of hexadecanol and hexadecyl palmitate in benzene against water.

Temperature	Concn. of each component (mol/l)	γ (dyne/cm)	γ (for hexadecanol alone at the concn. in column 2)
20°	0.0250	32.3	32.6
	0.0500	30.6	31.0
	0.0650	29.9	30.1
	0.0800	29.4	29.4
	0.1000	28.3	28.4
60°	0.0250	30.0	30.3
	0.0500	29.3	29.4
	0.0650	29.1	29.1
	0.0800	28.8	28.8
	0.1000	28.3	28.4

Effect of electrolytes on the interfacial tension

First, the interfacial tension of an N/10 solution of A.R. sodium hydroxide in deionized water against redistilled benzene was determined; a marked ageing effect was observed.   To make sure that the ageing effect was not due to transfer of liquid across the interface, the two phases were shaken together for 5 min, allowed to separate at 20°, and the interfacial tension was redetermined using the mutually saturated phases.   The results (*Fig. 5*, curve 4) are not significantly different.   To determine

whether the lowering in interfacial tension could be attributed to impurities, the following experiments were carried out.

(1) Pellets of sodium hydroxide (A.R. grade) were washed with 50 ml portions of deionized water until about half the solid had dissolved. The residue, which did not contain any detectable amount of carbonate, was dissolved in deionized water, and after its concentration had been determined by titration, its interfacial tension against benzene was determined (*Fig. 5*).
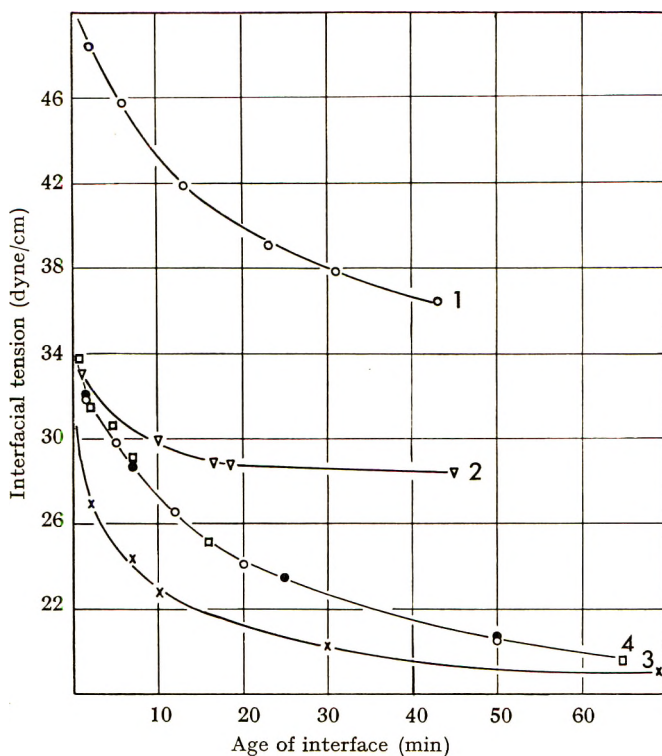
Figure 5

Effect of sodium hydroxide on the oil/water interfacial tension

1.	0.01N	NaOH/cyclohexane ; at 20°
2.	0.01N	NaOH/benzene (washed with NaOH solution) ; 20°
3.	0.1112N	NaOH/benzene ; 40°
4. ⎧ O 0.10N		NaOH/benzene ; 20°
⎨ ● 0.10N		NaOH/benzene, 20° (phases mutually saturated)
⎩ □ 0.10N		NaOH (Na₂CO₃-free)/benzene ; 20°

(2) Redistilled benzene (50 ml) was shaken with a concentrated solution of sodium hydroxide (A.R. grade; 50 ml) for 20 min and the solutions were allowed to stand for 30 min. About 75% of the benzene layer was

drawn off, and the treatment repeated three more times. The benzene was then washed with deionized water (5 × 50 ml) ; the last two washings were neutral. The interfacial tensions of this specially prepared sample of benzene against aqueous alkali is shown in *Fig. 5*. It is seen that there is still a marked time-dependent fall in the interfacial tension. A second system containing pure cyclohexane (spectroscopic grade) also showed a progressively diminishing interfacial tension against aqueous alkali with time (*Fig. 5*).

Fig. 6 shows that the interfacial tension of benzene against aqueous alkaline solutions depends upon the concentration of the alkali. The inverse linear relation between the interfacial tension and the hydroxyl ion concentration suggests that the adsorbed species is the hydroxyl ion.
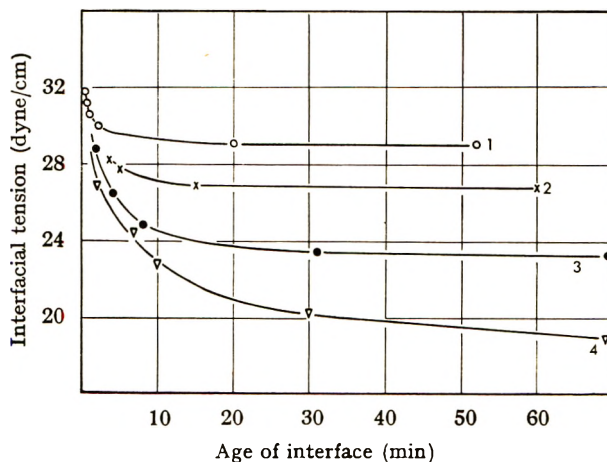
Figure 6

Interfacial tensions of aqueous alkaline solutions against benzene; at 40°.

    1. 0.0156N NaOH
    2. 0.0312N NaOH
    3. 0.0624N NaOH
    4. 0.1248N NaOH

Solutions (M/20) of sodium carbonate, sodium bicarbonate, sodium borate and sodium hydroxide (all A.R. grade) were made in deionized water and their pH values were determined using a Cambridge bench pH meter. *Fig. 7* shows the interfacial tensions of the solutions against redistilled benzene.
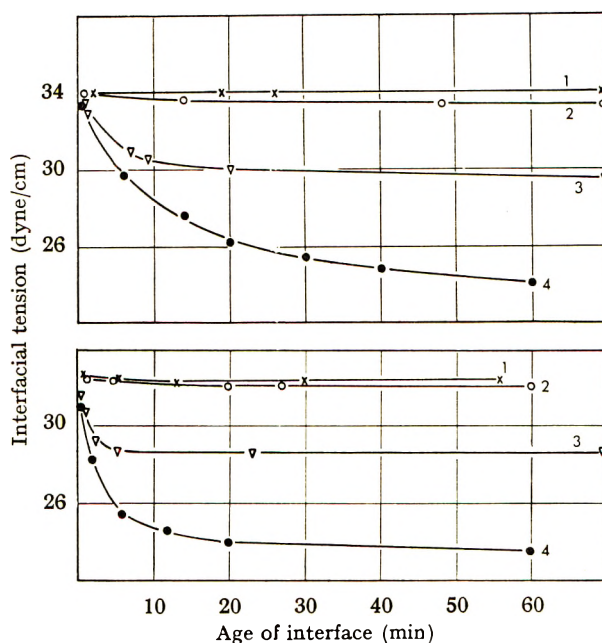
Figure 7

Interfacial tensions of M/20 salt solutions against benzene; at 20° (upper) and 40° (lower).
1. Sodium bicarbonate ; pH 8.2
2. Sodium borate ; pH 9.2
3. Sodium carbonate ; pH 11.0
4. Sodium hydroxide ; pH 11.8

Effects of sodium chloride

Sodium chloride added to the aqueous phase raises the interfacial tension, but if the aqueous phase contains sodium hydroxide as well, then the interfacial tension rapidly decreases to a lower value than with the corresponding concentration of sodium hydroxide alone. *Table IV* shows that sodium chloride has little effect on the interfacial tensions of benzene solutions of cholesterol and cholesteryl stearate ; the observations suggest that the interfacial tension is increased slightly.

Table IV   Equilibrium interfacial tensions of benzene solutions containing cholesterol and cholesteryl stearate against 4M aqueous sodium chloride, and against water.

Temperature °C	Cholesterol (mol/l)	Ester (mol/l)	γ for 4M NaCl (dyne/cm)	γ for water (dyne/cm)
20	0.0400	0	24.1	23.9
60	0.0400	0	28.4	29.0
60	0	0.0800	30.5	30.6
60	0	0.0600	31.2	30.8
60	0	0.0400	32.0	30.9

Fig. 8 shows that the interfacial tensions of benzene solutions of cholesterol and cholesteryl stearate against alkali are markedly affected by the presence of sodium chloride in the systems. Corresponding systems containing hexadecanol and hexadecyl palmitate (*Fig. 9*) show the same marked lowering in the interfacial tension against aqueous alkali containing sodium chloride.
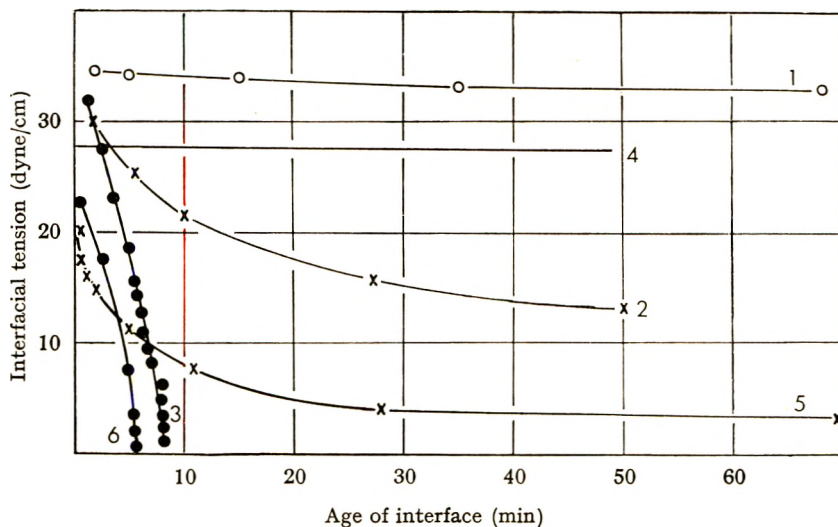
Figure 8

Effect of sodium chloride and sodium hydroxide upon the interfacial tensions of benzene solutions of cholesterol and cholesteryl stearate, against water; at 20°.

1. 0.1M cholesteryl stearate/water
2. 0.1M cholesteryl stearate/0.05N NaOH
3. 0.1M cholesteryl stearate/0.05N NaOH + 3.2M NaCl
4. 0.05M cholesterol/water
5. 0.05M cholesterol/0.05N NaOH
6. 0.05M cholesterol/0.05N NaOH + 3.2M NaCl

Effect of hydrogen ions on the interfacial tension

We found that the interfacial tensions of benzene and of solutions of cholesterol and of cholesteryl stearate against water were raised by the addition of sulphuric acid to the aqueous phase. Hence, the hydrogen ion is negatively adsorbed.
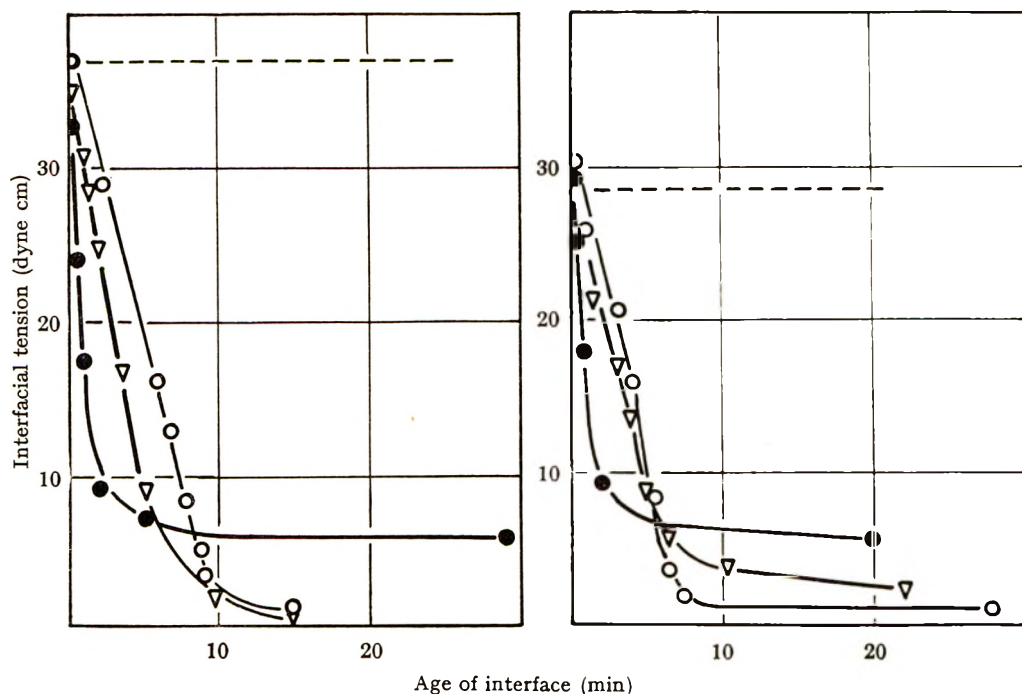
Figure 9

Interfacial tensions of 0.1 molar solutions of hexadecyl palmitate (left) and hexadecanol (right) in benzene against aqueous solutions of 3.2M sodium chloride plus 0.05N sodium hydroxide.

    ○   at 20°
    ▽   at 40°
    ●   at 60°
- - - - - against water at 20°

DISCUSSION

The most striking conclusions from these observations are that the wax-ester is not surface active, and that the ester does not form a surface active complex with the alcohol. If hydroxyl ions or hydrogen ions are preferentially adsorbed, then alkalis or acids must lower the oil/water interfacial tension. Previous investigations (12,13) have shown, and we have confirmed, that the hydrogen ion is negatively adsorbed. Correspondingly, the hydrogen ion catalyzed heterogeneous hydrolysis of esters is very slow (3). Experimental evidence for the adsorption of the hydroxyl ion at the oil/water interface is conflicting; according to Fahrenwald (14), Dickinson (15), and Roberts (16), it is positively adsorbed but according to Harkins (17) and Reynolds (18) it is not. Some workers take the view that the hydroxyl ion should be negatively adsorbed at the oil/water

interface so they attribute the contrary evidence to the presence of residual traces of impurities in the reagents. We find that in spite of all reasonable precautions in the purification and handling of the reagents, with real materials (as opposed to hypothetically pure materials), alkalis bring about a lowering of the oil/water interfacial tension (*Figs. 6 and 7*).

The conclusion that the hydroxyl ion is surface active, conflicts with the kinetic aspect of the adsorption theory. The theory demands that a surface active species be adsorbed rapidly; a slow change in interfacial tension indicating either a reorientation of the adsorbed species in the interface (an unlikely explanation for the behaviour of the hydroxyl ion) or that a surface active substance is being formed *in situ*. Any such reaction that may occur in the system must involve the hydroxyl ion because it is only in its presence that ageing effects are observed. The other participant in this hypothetical reaction could occur in any of the three types of starting material; each possibility may be critically assessed in the light of the experimental work.

(i) *Sodium hydroxide :* It is unlikely that the effects observed with sodium bicarbonate, sodium carbonate, sodium borate, sodium hydroxide and washed sodium hydroxide, the magnitudes of which are related to the pH values of the solutions (*Fig. 7*), could arise from the appropriate degrees of contamination of all five materials.

(ii) *Oil phase :* Because the same effects were observed with benzene, alkali-washed benzene and cyclohexane it is unlikely that the oil phase contains impurities.

(iii) *Water :* Observations were repeated with the same stocks of benzene and aqueous alkali over a period of two days. If the alkali were to react with impurities in the water, the old stock solutions should be surface active. In fact, the measurements were reproducible, showing that surface active substances are not generated by the action of sodium hydroxide on impurities in the water.

Hence, despite the conflict with the theoretical view, we are led to the conclusion that the hydroxyl ion is slowly adsorbed at the oil/water interface. It is of interest to note that the results of the earlier authors fall into two groups according to the technique used. Those who used methods that allow the ageing effect to be studied conclude that the hydroxyl ion is slowly adsorbed whereas those authors who did not study ageing effects state that the hydroxyl ion is not surface active.

Alkaline hydrolysis of wax-esters may be attempted in either o/w or w/o emulsions. From the very extensive literature on the behaviour

of surface active compounds, a few general principles have come to be accepted. Those concerning the stabilization of emulsions are briefly summarised below. Stabilization of an o/w emulsion requires the presence of a monolayer of emulsifying agent at the interface. The monolayer is usually charged, but whether it is condensed or expanded is not of primary importance. For the stabilization of w/o emulsions the emulsifying agent should be uncharged and the constituent molecules must possess a considerable degree of lateral cohesion so that a condensed, fairly rigid interfacial monolayer is formed. Apart from the differences in charge and in lateral cohesion, the interfaces are regarded as essentially similar. It is now clear that enough evidence has been accumulated to show that the interfaces in the two types of emulsion are quite different. Thus, although wax-esters are not surface active, nor do they associate in the interface with wax-alcohols, they affect the emulsifying power of the alcohol. Hence, the interface in w/o emulsions cannot be as simply constituted as is generally supposed. The relation between the magnitude of the effect and the molecular chain-length of the ester implies that the ester is a structural unit in the interfacial phase. The optical properties of w/o emulsions suggest that the interfacial phase is a liquid-crystalline system which, in some circumstances, may extend throughout the oil phase (20).

In the simplest o/w emulsion hydrolysis, the oil phase consists of molten ester and the aqueous phase is a solution of an alkali-metal hydroxide in water. The ester is not surface active so, irrespective of the activity of the hydroxyl ion, hydrolysis will take place only when an ester molecule and a hydroxyl ion participate in a random but suitably oriented encounter in the interface. Hence, hydrolysis will be very slow, and it cannot be substantially increased by the addition of a wax-alcohol to the system because ester/alcohol complexes are not formed in the interface. Addition of a wax-alcohol may increase the rate of hydrolysis slightly through its ability to increase the total area of the interface of the emulsion, but even when the addition of an emulsifying agent does cause an improvement in the quality of the emulsion, the hydrolysis cannot be brought to completion because the surface active products of the reaction (the wax-alcohol and the soap) occupy the interface and very effectively screen the ester. This interpretation is in complete accord with the observations on the rates of hydrolysis of wax-esters in o/w emulsions (19).

In w/o emulsion hydrolyses, emulsions are usually preformed because there is no possibility of agitating the mixture (as there is for o/w emulsions)

by allowing the aqueous phase to boil. Alternatively, the unstabilized emulsion may be stirred continuously during the early part of the hydrolysis. The simplest method is to stabilize the emulsion long enough to allow the reaction to begin and for this purpose an emulsifying agent is added, the most appropriate being the wax-alcohol. The resulting interface is fairly rigid so that molecular translations in the interface are far less likely than in the o/w emulsion interface under the same conditions. In spite of the greater interfacial rigidity, the hydrolysis not only proceeds to completion, it also proceeds more rapidly than in o/w emulsions. Hence, the w/o emulsion interfacial phase must be capable of adsorbing the hydroxyl ion. All the other observations on the kinetics of hydrolysis in w/o emulsions follow from this premise. For example, as the hydrolysis proceeds, wax-alcohol is liberated from the ester and this, in turn, increases the amount of ester that can be brought into the liquid-crystalline phase. Correspondingly, the kinetic curves (3) show that the hydrolyses are auto-catalytic until about 70% of the ester has been hydrolysed. Similarly, the known catalytic effect of sodium chloride on the hydrolysis is only to be expected because the salt lowers the interfacial tensions of alkaline systems.

CONCLUSION

The extremely weak surface activity of the wax-ester is, by itself, a sufficient explanation of the difficulty encountered in hydrolysing wax-esters in o/w emulsions. In w/o emulsions, however, the hydrolytic mechanism requires that the hydroxyl ion should be able to penetrate into the interfacial phase. Why the same system should form interfacial phases having different structures is not clear. This problem as well as the details of the molecular organization of the w/o emulsion interfacial phase are interesting research projects which remain to be tackled.

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DISCUSSION

MR. L. I. CONRAD: The work in our laboratory on lanolin derivatives certainly confirms your observations on the lack of surface activity on the part of the wax esters. We have been particularly concerned with the participation of the wax esters in association phenomena at the interfaces of cosmetic emulsions. In your investigations on hydrolysis in emulsions have you found any effects of the lanolin free fatty acids on the rate of hydrolysis in either o/w or w/o emulsions?

I would also like to ask about the possible effect of hydrogen ion as opposed to hydroxyl ion on the hydrolysis of wax esters such as lanolin.

DR. TRUTER: First, let me say something about the fatty acids. If lanolin fatty acids are added to the wool wax esters and the hydrolysis is attempted by the ordinary method, i.e., as an o/w emulsion, the effect is almost negligible. There is, perhaps, a slight initial increase in the rate of hydrolysis but the reaction will proceed to about 40% and then come to a halt. With invert emulsions the effect is catalytic; the reaction is faster initially and reaches completion in a shorter time.

The answer to the second question is that hydrolysis cannot be brought about using the hydrogen ion in either type of emulsion. Correspondingly, we found that the interfacial tension of a system was increased by the addition of acid. In this respect acids behave like neutral electrolytes. The hydrogen ion is not surface active.

MR. H. E. GARRETT: I find it incredible that the hydroxyl ion should be adsorbed slowly at an interface such as a benzene-water interface. With respect I suggest that what you are really observing is the leaching of some material from your associated apparatus, the glassware or whatever your equipment is made up of, even *Pyrex* is not a safe material.

DR. TRUTER: I accept this sort of criticism because it is obvious that there is something wrong somewhere. Although we have been at great pains to make sure that impurity is not the explanation, there may be something we have overlooked. Nevertheless, even if we accept the possibility of leaching, we are still forced back to this fundamental question: If the reactants are still in separate phases, and neither reactant is surface active, why does the hydrolysis proceed to completion in a w/o emulsion but not in an o/w emulsion?

MR. H. E. GARRETT: I agree that the changes in interfacial tensions with time are not due to impurities in the hydrocarbons or in the caustic soda used.

DR. TRUTER: This is the most difficult of all our observations to explain, i.e. the *slow* fall in interfacial tension of systems containing the hydroxyl ion. In our experiments we used sodium hydroxide, purified sodium hydroxide, sodium bicarbonate, sodium carbonate and sodium borate and in all cases the observed lowering of

interfacial tension was proportional to the hydroxyl ion concentration in the aqueous solution. This, to my mind, excludes the possibility of impurities in the alkaline materials. Further, the fact that sodium chloride behaves in the expected manner suggests that the method of packing the chemicals does not introduce impurities. We have tested water purified by resin deionization and by double distillation in the standard manner and we obtained the same observations with different samples of water. We have examined cyclohexane, benzene and benzene purified by various methods and the effects are present throughout. Finally, we have to consider the possibility of some sort of leaching from the apparatus. If leaching takes place, it must be regarded as an apparatus factor and I find it hard to believe that it happens only in the presence of the hydroxyl ion, and that it is catalysed by sodium chloride (*Fig. 8*).

MR. H. E. GARRETT: I would accept all that you say about having proved that impurities are not present in your materials, and I would agree with you that this throws the responsibility for these changes on the apparatus. I think the fact that you are getting these effects with caustic materials or alkaline materials suggests very strongly that it is glassware which is the cause of the trouble. You presumably have your tip in a small cell to avoid evaporation troubles, and this means that your surface to volume ratio, glassware to solution, will be quite high.

DR. TRUTER: In the experimental arrangement, the aqueous solution is contained in the pipette. The possibility of a reaction between the aqueous alkali and the stainless steel capillary or the glass of the syringe cannot be discounted, though in our opinion it is unlikely. Because there is a discrepancy between theory and practice we must be careful not to discard any criticism without giving it due consideration. Whether the explanation lies in leaching or somewhere else, we just do not know.

DR. TRUTER'S ADDENDUM: We know that the structure of the o/w and w/o emulsion interfaces are different. One consequence of the difference is that in w/o emulsion hydrolyses the non-surface active esters and the hydroxyl ion, which has questionable surface activity, are able to come into contact very easily. We suggest that the interface is able to adsorb hydroxyl ions. The fundamental question is: What features of the structure of the w/o emulsion interface allow this to happen?

An Approach to Emulsion Formulation

B. W. BURT*

Presented at the Symposium on "Emulsions", organized by the Society of Cosmetic Chemists of Great Britain at Harrogate, Yorks, on 31st March 1965.

Synopsis—Two series of experiments dealing with heterogeneous systems are reported ; the first concerns mixtures of cresols, soap and water and emphasizes the importance of phase identification. Original work with *o*-, *m*- and *p*cresols is reported. The second series concerns the stability of emulsions of oil, water and a pair of nonionic emulgents ; the results tend to confirm the usefulness of the HLB concept.

The paper concludes with a discussion of the place of phase equilibria in the formulation and theory of emulsions.

Two separate series of experiments are described, both being work undertaken to develop practical exercises suitable for undergraduate and postgraduate teaching. Taken together they represent an attempt to link the academic approach to phase equilibria with the practical problems of emulsion formulation. The aim is to attempt to find a method of approach which will give the formulator greater insight into his practical problems.

The first series of experiments are arranged with the objective of elucidating the formulation of Cresol and Soap Solution B.P. (*Lysol*). It is of special interest to show the relationships between solubilized and emulsified systems. For these experiments the soap is made *in situ* by mixing oleic acid dissolved in the cresol, with aqueous solutions of sodium hydroxide. A number of mixtures are made to cover areas of a ternary phase diagram in which phase changes may take place. The compositions at which phase changes occur are found by dilution techniques using water

*School of Pharmacy, Chelsea College of Science and Technology, London, S.W.3.

and cresol as the diluents.   For student work a detailed plan with the most profitable dilution steps is laid down.   After each dilution the mixture is observed carefully and the number, type and characteristics of the phases present are noted.   It may be necessary to centrifuge heterogeneous mixtures in order to identify and note the number of phases found; microscopic and macroscopic examination is often required to detect birefringent anisotrophic phases.   The separated phases can be analysed for cresol and water content, although this is not part of the undergraduate exercise.

The results obtained during the development of the exercise are shown in *Fig. 1*.   It is a phase diagram characteristic of mixture of surfactant, aqueous phase and amphiphile and should be compared with the well known phase diagrams of Devichian (1).
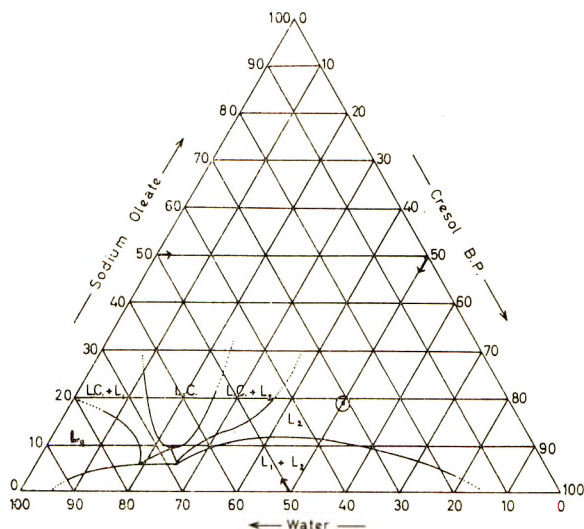
Figure 1

Phase equilibria diagram for sodium oleate + Cresol, B.P. + water.

L_1 = clear isotropic aqueous phase
L_2 = clear isotropic organic liquid phase
L.C.   = anisotropic liquid crystal phase
$L_1 + L_2$ = opaque emulsion
L.C. $+ L_1$ and
      L.C. $+ L_2$ = opaque immiscible mixtures
⊙   = composition of Lysol B.P.

The particular properties and advantages of the ternary phase diagram are well discussed by Ricci (2), Mulley (3), and others.   One advantage is that the dilution of a mixture with one of the components is represented by a line joining the composition of the mixture with the corner of the diagram

representing 100% of the diluting component. Thus the composition for
Lysol is shown in *Fig. 1*; now it can be seen that when water is added the
dilution must pass through an area of non-homogeneous mixtures. In
this instance the product does not contain glycerin which would be present
if the soap had been prepared by the method of saponification of a vege-
table oil; the presence of glycerin would open a miscibility gap similar to
that shown in *Fig. 3*. It is of interest to consider what would result from
the addition of further cresol to *Lysol*; as a solubilized product it would
seem that there must be a limit to the amount of cresol which could be
added before it would be in excess of its solubility. Inspection of the
phase diagram shows, however, that *Lysol* is miscible with cresol in all
proportions.
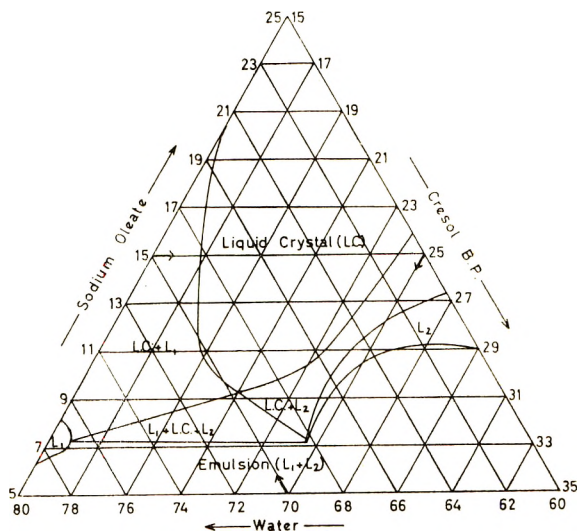
Figure 2

Phase equilibria diagram of sodium oleate + cresol B.P. + water ; detail of *Fig. 1* to show
three phases in equilibrium, L_1 + L.C. + L_2, letters as in *Fig. 1*.

For the present discussion, however, the interest is in heterogeneous
parts of the system. Just as the diagram shows how to formulate solubil-
ized products, and to avoid emulsified systems, so it can be used for the
converse purpose. If a stable emulsion could be thus formulated there
might be considerable advantages in bactericidal activity of the diluted
product. Even more important, however, is the relationship of the
classical emulsions area to other areas of heterogeneous mixtures. Formu-
lation investigations of mixtures in the triangular region shown enlarged in
Fig. 2 would be very confusing without the insight given by this presenta-

tion.   This is particularly important because it would seem that many emulsions are much more complicated than simple liquid/liquid mixtures and may pay investigating by similar procedures.   The fact that cresol and soap solution made in this way is not homogeneous through all stages of dilution with water is unexpected as this would mean that such a product does not comply with the official dilution requirements.   Even the absence of glycerin seemed insufficient as an explanation.   Further experiments sometimes confirmed this diagram while others showed a miscibility gap allowing a completely clear dilution of the B.P. product with water.
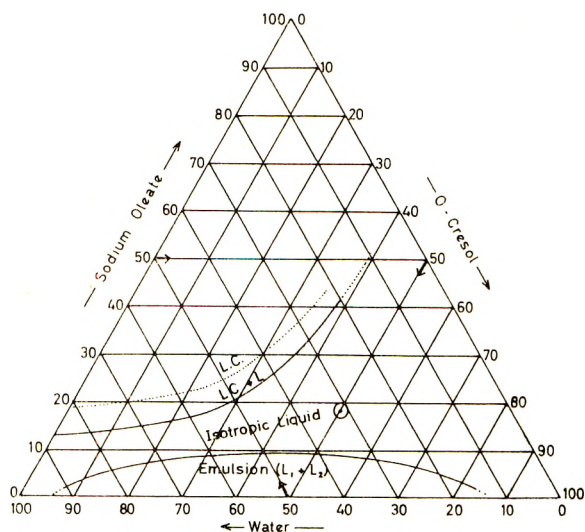
Figure 3
Phase equilibria diagram sodium oleate + ocresol + water ; letters as in *Fig. 1.*

In an attempt to resolve this situation a further series of experiments were made using a purified sample of oleic acid, and the separated isomers of cresol.   The results are shown in *Figs. 3, 4* and *5* where it can be seen that the *p*cresol isomer is mainly responsible for the absence of complete miscibility on dilution with water of cresol and soap solution made by this method.   Further it can be seen that the emulsion areas ($L_1 + L_2$) remain much the same for all these isomers; it is the areas involving the liquid crystalline mesophase (L.C.) which show big differences between the isomers.   Viscosity measurements of these isomers in soap solutions by Angelescu *et al* (4,5) would suggest the presence of a mesophase at about the concentrations found in this work and also confirm the tendency to mesophase formation with the isomers to be in the order (high to low) *p-, m-, o*cresol.
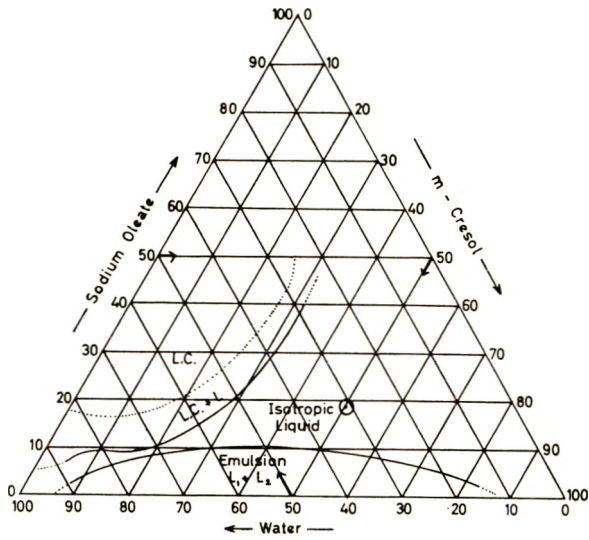
Figure 4

Phase equilibria diagram sodium oleate + mcresol + water ; letters as in *Fig. 1*.
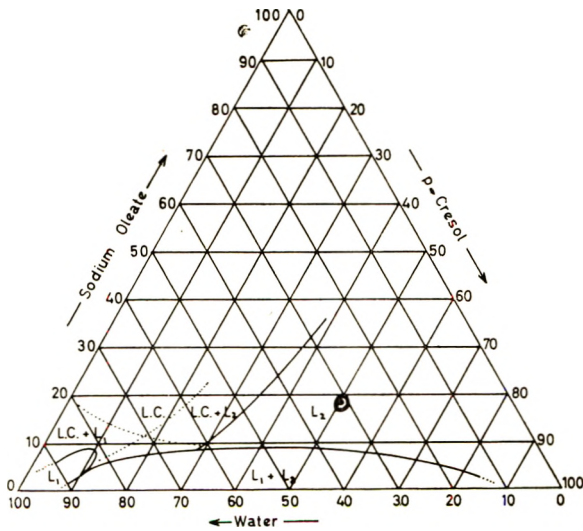
Figure 5

Phase equilibria diagram sodium oleate + pcresol + water ; letters as in *Fig. 1*.

From these experiments the importance of attempting to identify the phases present in heterogeneous systems can be appreciated, and the phase relationships of mixtures of the three components better understood.   It

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should be noted that this is somewhat different from simply the mathematical advantage gained by the triangular diagram representation which has been clearly demonstrated as a general aid to formulation by James and Goldemberg (6), and applied specifically to emulsion problems by Salisbury *et al* (7).

The second series of experiments were planned with the intention of applying the concepts and methods of the previous experiments to the formulation of the more classical emulsion type. The problem set here was to attempt to elucidate the formulation of emulsions of paraffin oil and water using a pair of nonionic emulgents such as *Tween 20* and *Arlacel C*. There are four components to be considered, and for a complete representation of mixtures of these a three-dimensional tetrahedron is necessary. Such a structure is shown in *Fig. 6*, and the five small triangles, each of which represents experimental areas of specified oil concentrations, are
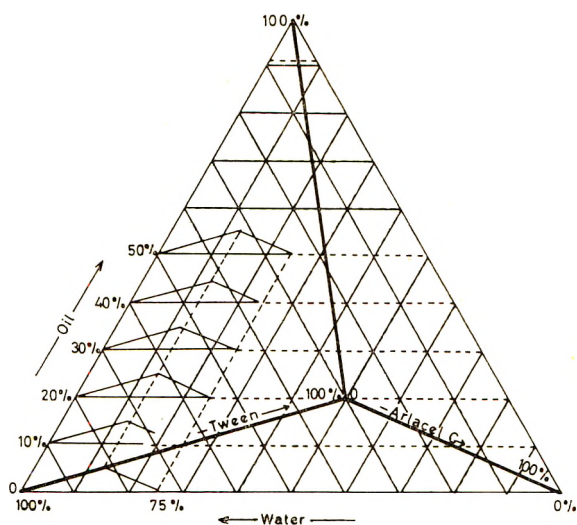
Figure 6

Three-dimensional tetrahedron representing mixtures of *Tween 20*, *Arlacel C*, water and liquid paraffin.

also shown. These triangles when isolated from the tetrahedron are shown in *Figs. 7–11*. Thus constructed, the individual triangles have mathematical properties especially useful for such experiments. Firstly, straight lines radiating from the bottom left-hand corner of the triangle (0 per cent *Tween 20*) represent mixtures which contain constant ratios of *Tween 20* and *Arlacel C*; for example, mixtures lying on line D in all the diagrams will contain varying amounts of a mixture of equal
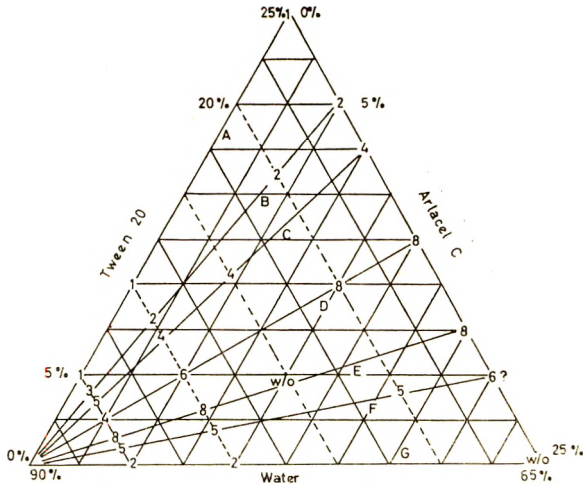
Figure 7

10% Oil

Composition diagram of mixtures all containing 10% liquid paraffin ; the other components are *Tween 20, Arlacel C* and water. Letters refer to HLB of lines radiating from bottom left-hand corner ; figures within the diagram represent the grade of the o/w emulsions from 1 = very poor to 9 = very good. W/o emulsions are not graded but the type is noted ; when there is doubt as to type a question mark is added. The dotted lines represent lines along which the total amount of emulgents is same, viz. 5%, 10%, 15%, 20% or 25%.
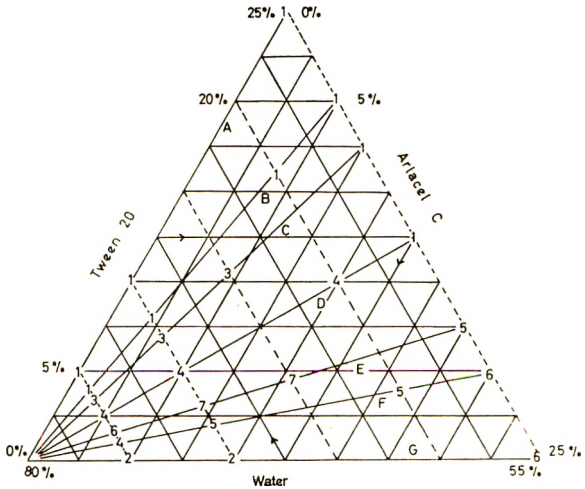
Figure 8

20% Oil

Composition diagram of mixtures all containing 20% of liquid paraffin: other components, figures and letters as in *Fig. 7*.
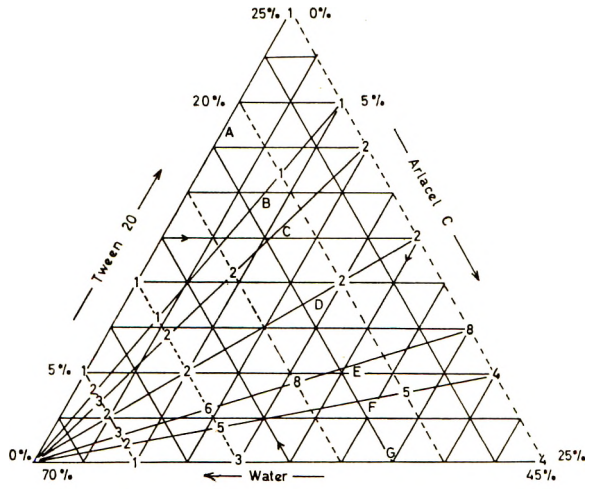
Figure 9

30% Oil

Composition diagram of mixtures all containing 30% liquid paraffin ; other components, figures and letters as in *Fig. 7*.
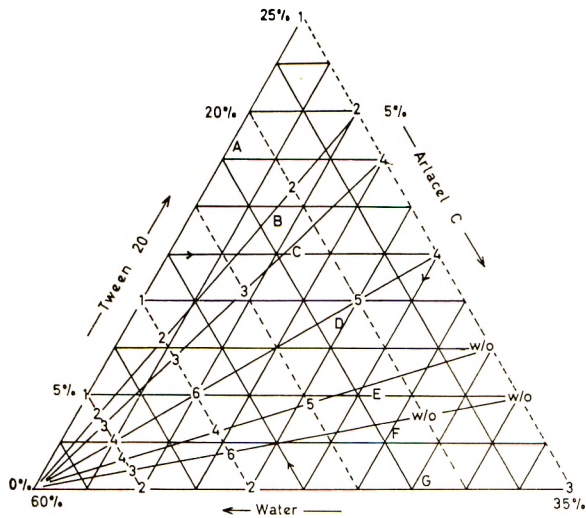
Figure 10

40% Oil

Composition diagram of mixtures all containing 40% liquid paraffin ; other components figures and letters as in *Fig. 7*.
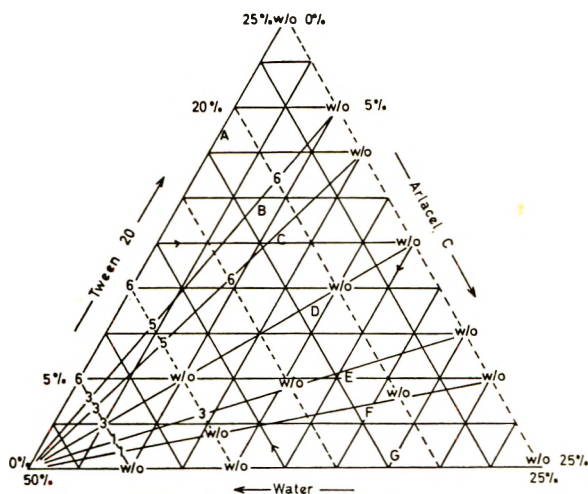
Figure 11
50% Oil

Composition diagram of mixtures all containing 50% liquid paraffin ; other components, figures and letters as in *Fig. 7*.

proportions of *Tween 20* and *Arlacel C*. Each line represents particular ratios of the emulgents and is thus a line of constant Hydrophil-Lipophil Balance (HLB). In the same way other lines can be arbitrarily chosen to give a suitable range of HLBs. In this series *Table I* shows the HLBs of the lines A to G on the diagrams. The second point of geometry to note is that a line crossing the triangle parallel to the right-hand side represents mixtures containing the same total amounts of *Tween 20* and *Arlacel C*. These are dotted lines on the diagrams and are chosen at 5, 10, 15, 20 and 25% of total emulgent levels. For the experimental formulae, mixtures were chosen which were at intersections of these HLB and total emulgent concentration lines.

Table I

Line letter	A	B	C	D	E	F	G
Weight ratios of *Tween 20*, *Arlacel C*.	1 0	0·8 0·2	0·7 0·3	0·5 0·5	0·3 0·7	0·2 0·8	0 1
HLB	16·7	14·1	12·8	10·2	7·6	6·3	3·7

The general plan of the practical work is first to equilibrate the mixture of components by heating at 60°C for an hour with intermittent shaking.

The containers are then placed in a shaking device and well agitated continuously until the temperature falls to about 30°C. The mixtures are then passed twice through an electrically driven, spring-loaded valve homogenizer, and collected ready for examination and storage. The oil phase was stained with a small quantity of a red dye. The objective set for the series is to find suitable formulations for o/w emulsions and an arbitrary scale of marks from 1, for a very poor product, to 9, for a very good one, is laid down. The figures within the triangles represent this evaluation of the products at these compositions. The usual tests for emulsion type are applied. The evaluations finally made after eight weeks' storage are those recorded; colour photographs were also taken at this time.

The results can be said to give general confirmation of the usefulness of the HLB concept in choosing a suitable blend of these emulgents for o/w emulsions of liquid paraffin and water. For emulsions with oil concentrations up to as much as 30% the best series of results lie on line E (HLB = 7.6). For 40% oil it would be safer to move to a higher HLB, say on line D (HLB = 10.2) to avoid the possibility of a w/o emulsion occurring due to variation in techniques of production. At 50% oil concentration many of the mixtures are of the w/o type. This is due mainly to the high oil to water ratio which results when high concentrations of emulgents are used, and there would appear to be no satisfactory product of an o/w type in this series.

Attention must be drawn, however, to the extreme difficulty of determining the emulsion type of many of these products. Few of the usual tests for emulsion type give reliable positive results. Conductivity was the test most relied on in these experiments; a trace of electrolyte is included in the aqueous phase for this purpose, but even this method can give equivocal results. From the entirely practical point of view, however, this procedure can be used to select products of likely interest to the formulator.

It is well known that many commercial nonionic materials do not exhibit a well-defined birefringence. Thus mixtures of these two surfactants with water, with no oil present show birefringence clearly only when the total concentration of the emulgents approaches 40%; this is about the ratio of emulgent to water as occurs in the experimental emulsions when 50% oil and 25% emulgent are present. Many mixtures of these emulgents with water have gel-like consistency although birefringence is not detectable. Many of the emulsions exhibit similar gel properties but it has not so far been possible to establish phase diagrams of the type

shown for the soap and cresol experiments. Nor has it been possible to isolate phases from the emulsions for inspection, but that this is highly desirable is obvious; the techniques most likely to be of value in the resolution of this problem are high speed centrifugation, and thermal analysis. The microscopic examination of many of these products together with their rheological properties would suggest that in many cases a gel is often the continuous phase in which is dispersed excess of either the aqueous or oily phase, or even both. This is a very different situation to the classical concepts of emulsion theory. No special mathematical benefits are claimed for the presentation of the results in this way; they can be appraised just as readily in tabular form or in rectilinear diagrams. It is rather an approach to the formulation of emulsions against a background of phase equilibria, which such a representation makes it possible to conceive.

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DISCUSSION

Mr. P. Sherman: Have you studied the influence of emulsifier concentration on the type of emulsion obtained or on the stability of emulsion at a constant HLB value?

The Lecturer: No, I cannot say that we have done this other than indicated in the paper. In the systems that we looked at there is a mathematical disadvantage in arranging the experiments as they have been done, choosing particular oil levels. It would have been better to keep phase volume ratios constant as far as one can in these situations and that would have meant all the triangles sloped downwards, but it would have been confusing, at any rate, as a teaching experiment. What happens mostly is that as the emulgent concentration increases so the water concentration decreases, and you have a slightly different phase volume ratio situation.

MR. P. SHERMAN: I raised this question because I think this whole concept of HLB is in danger of being over-emphasized. The volume concentration ratio can be kept constant by adjusting it slightly as you increase the emulsifying concentration, but particularly when you are dealing with the *Tweens* which, although they give o/w emulsions, are nevertheless only dispersable in the water phase and actually soluble in the oil phase. If you have fairly concentrated volume concentrations of dispersed phase and disperse your *Tween* in the aqueous phase process you actually obtain a transfer of the emulsifier to the oil phase during the emulsification so it is distributed between the two phases. Alternatively you can start your emulsion by partitioning the emulsifier between the two phases. You do find, when the level of perhaps 5 to 6 % emulsifier is reached that inversions from the o/w type to the w/o occur, and this is one of the classical cases where the whole concept of HLB is breaking down.

THE LECTURER: This is correct, particularly when you are using *Span* or *Arlacel*. It seems to me that there is a big difference here between the classical approach to emulsion theory which involves interfacial films, monomolecular films, etc. In model systems, using extremely dilute emulgent concentrations you can show the importance of lipophil/hydrophil balance (8). This is an attempt to change the emphasis from the point of view of the theory of emulsions from terms of dilute solutions and monomolecular films at the surface, to the bulk phenomena, which I think has been very much neglected. In real products the total emulgent concentrations are at least 5 % with the nonionics. The concentration in the aqueous phase is often much higher than this, so that these gel systems, which have been noted quite often in the past, are really the continuous phase. The same transference argument crops up with soaps, e.g. sodium oleate is a classic o/w emulgent, and yet, if you increase the concentration enough, as in some liniments, for example, a w/o emulsion results. In the past, people have experimented with electrolyte and shown transference of soap into the oily phase, In a classical emulsion theory this would be the emulgent soluble in the oily phase, therefore the oily phase is the continuous phase, and so on. I think it is much more likely that the situation is a bulk phenomenon concerning liquid crystal. If you have a very thick gel-like liquid crystal you can disperse oil or water or even both, in that as with Lysol. That is the reason for including the Lysol experiments.

MR. R. L. STEPHENS: Have you not found that the Lysol soap system is particularly dependent on temperature? I seem to remember having done some similar experiments at one time and being very puzzled because I could not reproduce my results; it was merely a matter of two or three degrees difference in the temperature of the laboratory from one day to another.

THE LECTURER: Yes, this is very true. I brought a three phase system with me, and was very sad to find this morning that the temperature had dropped and one of the phases had disappeared. If you are not careful to use a refrigerated centrifuge, the phases may change before your eyes.

MR. D. E. HERRING: Can you comment on the breaks that occur in the stability figures in *Fig. 10* at 10 % emulsifier level, i,e. 1, 2, 3, 6, 4, 6.

THE LECTURER: At 40 % concentration of oil the concentration of emulgent in water is becoming very high indeed, and it is extremely difficult to classify the products

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(8) Davies, J. T. *2nd Int. Congr. Surface Activity* **1** 426 (1957).

at all. Here it is a problem of product assessment. It is easier when more water is present, i.e. a more classical o/w system. How do you assess emulsions? What tests are you going to apply for a good or a bad emulsion? I find it is extremely difficult to have a system of emulsion assessment. The parameters of emulsion measurement are sadly in need of improvement before we can really make very much progress.

MR. D. E. HERRING: Would you explain the figures a little more?

THE LECTURER: What I really did here was to produce a series of drawings. Nine, for example, which was one of the best emulsions, did not have any free oil drops visible, no free aqueous drops, the light colour was continuous throughout, a.s.o. Eight would perhaps have a trace of free oil. Seven would have visible free oil in a thin layer, a.s.o. This is the system that the score was based on.

DR. H. ZIEGLER: Have you found any difference by using a different method of homogenization?

THE LECTURER: I have not done enough to really answer this. The particular pair of materials were chosen first of all to give a wide range of HLB. In practice one would not, I think, start from such a wide difference in HLBs. Secondly, I wanted to avoid the inclusion of solids as far as possible, because this would have made it even more confusing. These were the reasons for choosing the particular pair of emulgents. We added the ingredients to each other at about 60°, continued shaking until reasonably cool, and then passed twice through a piston homogenizer; we did not use an alternative homogenizer.

MR. R. GUCKLHORN: Did you correlate particle size with any other parameters?

THE LECTURER: No. This is very difficult, particularly with high concentrations.

Book reviews

RECENT PROGRESS IN SURFACE SCIENCE. Editors: J. F. Danielli, K. G. A. Pankhurst, A. C. Riddiford. Vol. 1. Pp. xii + 414 + Ill. 114/6. Vol. 2. Pp. xiv + 541 + Ill. 128/6. (1964). *Academic Press, New York and London.*

Surface science means different things to scientists of different disciplines. To some it is the phenomenon associated with spreading monolayers of surfactants on water. Many student chemists regard it as adsorption of gases on solids, while biologists consider it as active transport and adhesion of cells. All of them are quite correct, and this tremendous width of interest is reflected in the contents of the two volumes edited by Danielli, Pankhurst and Riddiford. All of the chapters are by acknowledged world experts and many of the chapters are of some relevance to cosmetic chemists.

The aim of the editors has been to report significant advances in selected fields during the period 1956–1961. Some authors had their material ready on time and the editors apologize to them for the delay in publication, which was caused by the difficulties of others. As a result of this the volumes are rather unbalanced. For instance, *Volume 2* contains a chapter on "Contact Angles" written by Elliott and Riddiford when the proceedings of the 3rd International Congress on Surface Activity (1960) were not available, while the following chapter on Emulsions by Davies gives references up to 1964, based mainly on Davies's own work. The ideas on emulsion type, stability to breaking and creaming, and to inversion, are new, providing a quantitative treatment which will ultimately enable much of the "mystique" to be removed from emulsion manufacture.

Kitchener's chapter on "Foams and Free Liquid Films" in *Volume 1* is in the same high vein, but here the quantitative aspects are less advanced. The theoretical treatment emphasizes the importance of the Marangoni effect and the surface dilational elastic modulus. The Marangoni effect arises from the fact that an expanding surface on a dilute solution of a surfactant has a somewhat higher surface tension than the static value for the solution. Conversely, a compressed surface develops a lower temporary tension than its surroundings. Hence, mechanical disturbances, whether in a longitudinal or transverse direction in the liquid film, are instantly met by a restoring force tending to annul the disturbance. The Marangoni effect therefore accounts for the fact that an optimum concentration for maximum foaming in a transient-foaming system is always found. If the solution is too dilute, the greatest possible differential tension is small; if the solution is too concentrated, the differential tension relaxes too rapidly, because of supply to surfactant by diffusion, for the restoring force to have time to counteract the disturbing force. Kitchener presents a sound theoretical picture but always emphasizes the practical importance of the work.

The chapter on Surface Viscosity, which starts *Volume 1*, serves to emphasize the lack of recent real progress in the field. After Kitchener on Foams, Haydon considers Electrical Double Layers in a purely theoretical treatment, which fails to emphasize many of the inadequacies of the work to date. Schuldiner emphasizes, in the chapter on Electrode Processes, the techniques now available for measurement of properties of electrodes and provides a comprehensive treatment of the hydrogen electrode. In a short chapter King manages to summarize adequately the vast amount of recent work on Corrosion. The chapter on Surface Active Agents by Black will disappoint many. Space is wasted on developments in inter-war years while biodegradable detergents have less than two pages. The remaining non-biological chapter is on Semiconductor Surfaces.

The biological work in *Volume 1* has three chapters on Cell Contacts, External Surfaces of Cells, and Bimolecular Lipid Membranes, which provide an excellent background to imminent developments in our knowledge of the skin. All the properties of the skin are determined by these three factors and our improved ability to modify our main substrate lies in a better understanding of them.

Turning now to *Volume 2*, besides the chapters on Emulsions and on Contact Angles already mentioned, the physical chemistry papers deal with Physical Adsorption at the Gas Solid Interface, Heterogeneous Catalysis and with Flotation, all of which are competent up-to-date reviews of our state of knowledge in the fields. The chapter on Genetic Control of Cell Surfaces has rather too much genetics and too little directly concerned with surfaces. The chapters on Physiology of Pinocytosis and on Plastron Respiration make fascinating reading. The two chapters on Cell Membranes bring us up-to-date on structural aspects (although omitting many of the biophysical aspects) and also sound a warning regarding electron microscopy. Many believe that the pictures taken represent the true state of affairs and it is only the better microscopists who continually warn us of possible artefacts.

We have, therefore, two volumes giving interesting accounts on many aspects of surface science. Each volume contains chapters on physical chemistry and on biological topics and they are recommended to those whose interests are sufficiently wide.

INTERPRETATION OF THE ULTRAVIOLET SPECTRA OF NATURAL PRODUCTS. A. I. Scott. Pp. x + 433 + Ill. (1964). *Pergamon Press, Oxford.* 84s.

This is essentially a pragmatic book – written by a practising natural product chemist, trained in the busy Bartonian school, in constant contact with steroid/terpene/alkaloid chemists. Ian Scott admits at the outset that he has not concerned himself with rigorous (or indeed hardly any!) theoretical treatment nor (in this book) with mechanistic discussion. Between the somewhat distant covers he has included a working guide to assist the organic chemist to devise his own structural diagnosis from UV spectroscopic measurements.

In a brief introduction, standard concepts and conventions are iterated and the basic electron excitation mechanisms are comprehensively analysed – albeit less digestibly than by Bladon (1) but this section improves on rereading. In the first

(1) Bladon, P., in Schwarz, J.C.P. ed. *Physical Methods in Organic Chemistry*, Chapter 4. (1964), Oliver and Boyd, Edinburgh.

full chapter, Professor Scott describes isolated chromophores. He shows that whilst meagre direct use can be made of absorption due to decoupling of lone pair electrons (i.e. n to sigma* transitions as in C–O, C–S, C–N or C–hal) which give rise to weak bands mainly in the inaccessible UV region, they may contribute useful background data for subtraction from new active chromophores. Isolated alkene/alkyne absorption, unless in a strongly hindered environment, is usually barely accessible too (185–205 mµ). The carbonyl group gets well-merited detailed attention: The weak band near 280 mµ arising from local (n→π*) excitation is examined in a variety of functions but its diagnostic value is limited to a number of specialized environments. A similar transition in C=N, N=N, N=O and C=S receives brief mention and examples are tabulated.

In the second chapter, Scott analyses the variety of intense absorption bands due to electron transfer (ET) between two or more conjugated chromophores. A clear exposition is given of the use of the Fiesers' (and some of the author's own) extensions of the well-known "Woodward rules," whereby may be predicted the absorption maxima for conjugated hetero- and homo-annular polyene and αβ-eneone systems. The effect, on the ET transition, of polar substitution and solvent interaction is considered and warning is given of the occurrence of some exceptions and contradictions. Attention is also given to variation in the wavelength of the low intensity (n→π*) bands of αβ-eneones and to other carbonyl functions, e.g. βγ-eneones and conjugated unsaturated lactones, amides, aldehydes, and nitriles, as well as cumulative unsaturation as in ketens and allenes.

It is unfortunate that comparable empirical correlation has yet to be achieved for the complex steric and electronic interactions that cause aromatic and heteroaromatic absorption spectra; study of closely related structures is necessary for reliable diagnosis. In the third chapter, Prof. Scott surveys in considerable detail common aromatic chromophore correlations including the diagnostic employment of variation in pH and solvent. Numerous examples are cited of phenols and their ethers, various nitrogen derivatives, higher aromatic systems and a variety of conjugated ethylene and carbonyl functions. O and S hetero-aromatic systems receive special attention in the fourth chapter; mention is made of benz-condensed and β- and αβ-substituted furan groupings which occur in a wide variety of natural products although–as Scott points out–NMR and IR spectroscopy are potentially more rewarding for these functions. Of wider significance are the UV spectra of the α- and γ-pyrone systems, particularly the naturally occurring coumarins, flavones and xanthones. Substances containing the thiophen ring are rare and only receive brief mention. The fifth chapter is devoted to a condensed account of mono-azine spectra – a topic worth a book in itself since it embraces by far the largest portion of the alkaloid field. Special reference is made to derivatives of pyrrole (including porphyrins and some examples of the numerous varieties of indole alkaloid), pyridine, quinoline and isoquinoline. Finally, polyazine spectra are examined in a short sixth chapter; examples are given of absorption maxima of pyrimidines, pyrazines, purines and pteridines.

Having dealt with the details of chromophore correlation, the second half of the book is concerned with applications to natural products. In Chapter 7, Dr. Charles Brooks (a colleague of Scott's from his London and Glasgow days) interpolates an account of spectrophotometry as an analytical tool, which includes the use of colour reactions in the assay of microgram quantities of biological products, studies of

reaction progress or equilibrium, and the determination of acid or base strength. Methods of transformation to another more appropriate substance are suggested where a suitable chromophore does not exist in the original structure.   Derivatives, colour reactions and changes with various reagents are all discussed with examples.

In the next chapter we reap the diagnostic harvest of the relationships established earlier in the book.   Prof. Scott emphasizes that the investigation of gross molecular structure ideally goes hand-in-hand with IR, NMR and mass spectroscopic evidence: The first two are concerned with localized features of the molecule whilst absorption spectra will better indicate the extended environment of (some of) these groups. He arbitrarily selects a series of examples of chromophoric groups of increasing complexity of interpretation to illustrate this thesis.   Most of these examples are given their own monograph in which both regular and anomalous behaviour are analysed.

From the consideration of individual chromophores within a complex molecular environment, Scott turns to the interpretation of composite spectra containing contributions from several independent functions.   Choosing examples – many from his own experience or cognate fields – he describes useful degradative or creative manipulations whereby the individual chromophores may be resolved.   He ranges over mould metabolites and antibiotics, lignans, constituents of shellac, aconite and related alkaloids, sesquiterpenes, terpenoid bitter principles – including a brief account of the deployment of spectral data in the elucidation of a citrous product all too familiar to this reviewer–and finally some anomalies noted by Bentley in the morphine series.

In a so-called "Appendix," Scott summarizes chromophoric environments found in a wide variety of steroid structures, refers to a number of diagnostically useful manipulations and tabulates a massive compendium of absorption maxima that have been published for steroids – the field in which so much of the early correlations were discussed.

This is a monumental – and in places not easily digestible – book, but it is packed with vital information, much of it conveniently tabulated; it offers a wider ranging empirical approach to UV spectral correlation than any existing work.   Some readers might cavil at the admixture of jocular prefaces and telegraphic descriptions; nevertheless the style is concise and generally consistent, although stated preferences – some of them by no means universally accepted conventions – are not always maintained.   This is not the book for the physicist nor for the instrumentalist: it IS warmly to be commended to all active organic chemists.   G. F. PHILLIPS

BAILEY'S INDUSTRIAL OIL AND FAT PRODUCTS.   3rd Edn.   D. Swern, Ed.   Pp. xiii + 1103 + Ill.   (1965).   *John Wiley & Sons, New York/London/Sydney.*   189s.

The cosmetic chemist depends to a very large extent upon materials derived from oils and fats and therefore one might expect a book with this title to be an invaluable source of information.   In this sense he will be disappointed since the "products" referred to in the title are not so much chemically derived materials as food products, etc.   In fact the number of materials mentioned which are of direct interest to the cosmetic chemist are very few and even these are usually treated very cursorily; more information will generally be found in the works on cosmetic materials and the pharmacopoeias.   The cosmetics industry is dismissed in a few

lines.   No mention at all is made of the commonly used fatty esters and even glycerol monostearate is included only in its context as a shortening agent in foodstuffs. Neither mineral oils nor waxes are covered.   One chapter is devoted to soap and surface-active agents, but this is rather sketchy and contains far less than the average cosmetic chemist requires to know about these materials.

Nevertheless the cosmetic chemist will find certain sections of this book rewarding reading.   In particular, a 19-page section of Chapter 2 contains an excellent discussion of atmospheric oxidation and rancidity; Chapter 3, on the physical properties of fats and fatty acids, contains much useful information; a part of Chapter 11 and Chapter 20 deal respectively with the phase behaviour of soaps and with soapmaking.

Essentially this volume is a review of the technology of animal and vegetable oils and fats and their principal uses.   Four authors have contributed: D. Swern, who also edited the book, K. F. Mattil, A. J. Stirton and F. A. Norris.   The treatment is elementary in its beginnings and extends through the structure and composition of fats and oils, reactions, physical properties, fats in the diet, sources, utilization and classification, and then the composition and characteristics of individual fats and oils.   Application to various food products, paints and varnishes, and other miscellaneous products is reviewed.

The last half of the book is a survey of oil and fat technology proper and this is first-class.   Handling, storage and grading are covered first followed by extraction, refining and bleaching, hydrogenation, deodorization, fat splitting and esterification/interesterification.   An interesting chapter on soapmaking, including a description of the more modern techniques, follows.   Chapters on fractionation, polymerization and isomerization, solidification, homogenization and emulsification conclude the volume.

Each chapter is adequately supported by references to original articles and a comprehensive subject index is appended.   The book is very well produced and remarkably free from typographical errors.   Subject to the limitations detailed in the first paragraph this volume could be a useful addition to the library providing as it does excellent background information on oils and fats processing.   R. P. REEVES.

1965-66 PROGRAMME
Lectures will be delivered on the following Thursdays:

7th October 1965.	3rd February 1966.
2nd December 1965.	31st March 1966.
6th January 1966.	

FILM EVENING: Thursday, 19th May 1966.

MEDAL LECTURE: Thursday, 3rd March 1966.

SOIREE: Saturday, 9th October 1965.

1966 DINNER AND DANCE: Saturday, 5th February 1966, at the Europa Hotel, Grosvenor Square, London W.1.

ANNUAL GENERAL MEETING: Monday, 23rd May 1966, at the Washington Hotel, Curzon Street, London, W.1.

SYMPOSIUM ON PHYSICAL METHODS

A Symposium on Physical Methods will be held at the Grand Hotel, Bristol, on 16th and 17th November 1965. Participation is permitted only when application has been made on the appropriate form, and the fee duly paid. This is £3 3s. for each participant who is a member of one of the Societies of Cosmetic Chemists affiliated to the I.F.S.C.C. The registration fee for non-members is £6 6s. Registration forms giving all details are available from the General Secretary, Mrs. D. Mott, 18 Warner Close, Harlington, Middx. **The closing date for registration is 18th October 1965.**

Tuesday, 16th November 1965

Afternoon

Chairman: A. Herzka, Esq., Hon. Editor

14.00 "Spectrophotometric methods for the rapid evaluation of the inactivation of anti-microbial agents."
M. R. W. BROWN, M.Sc., Ph.D., M.P.S., M.I.Biol. (*School of Pharmacy, Bristol College of Science and Technology*).

14.30 "Thin-layer chromatographic techniques in residue analysis."
J. THOMSON, Ph.D., A.H.-W.C., A.R.I.C. (*Laboratory of the Government Chemist London*).

15.00 TEA.

15.15 "Particle size analysis using Coulter counters."
R. W. LINES, B.Sc. (*Coulter Electronics Ltd., St. Albans*).

15.45 "Infra-red spectroscopy of aqueous detergent solutions."
M. A. PUTTNAM, B.Sc., Ph.D., A.R.I.C. (*Colgate-Palmolive Ltd., Salford*).

17.00-18.00 Display of apparatus and equipment at School of Pharmacy, Bristol College of Science and Technology, Ashley Down, Bristol 7.

20.30-22.30 Civic Reception by the Lord Mayor of Bristol, Alderman T. H. MARTIN, M.B.E., at the Council House, Bristol. (Informal Dress.)

Wednesday, 17th November 1965

Morning

Chairman: R. CLARK, ESQ., President

09.45 "Spectral slit width and other sources of error in U.V. spectrophotometry."
A. R. ROGERS, B.Pharm., B.Sc., Ph.D., F.R.I.C., F.P.S. (*School of Pharmacy. Brighton College of Technology*).

10.15 "Rheological studies of new cream bases with the Brookfield synchrolectric visco-meter."
Professor F. NEUWALD, Dir.rer.techn. (*Institute of Pharmaceutical Chemistry, University of Hamburg*).

10.45 COFFEE.

11.10 "The analysis of aerosol propellants."
R. J. BROOK, L.R.I.C. and B. D. JOYNER, A.R.I.C. (*Imperial Smelting Corporation, Avonmouth*).

11.40 "Fluorescent antibody studies in dermatology."
N. R. ROWELL, M.B., M.C.R.P. (*General Infirmary at Leeds*).

Afternoon

Chairman: Dr. A. W. MIDDLETON, Vice-President

14.00 "Preparative gas chromatography."
G. R. FITCH, M.Sc., A.R.I.C. (*Department of Chemistry and Biology, Bristol College of Science and Technology*).

14.30 "Techniques for assessing the rheological properties of toiletry and cosmetic products."
P. SHERMAN, M.Sc., F.R.I.C. (*Unilever Research Laboratory, Welwyn*).

15.00 "The relation between structure and properties in plastics used in packaging."
A. SHARPLES, B.Sc., Ph.D. (*Arthur D. Little Research Institute, Inveresk*).

15.30 Symposium ends.

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