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Note added in proof. Since completing this article, we have been informed by Dr. Peters that, in Ilford C2 emulsions exposed at 90,000 feet, he and Dr. Bradt have observed three events with the following characteristics. A particle, which they judge to be similar in mass to their τ -mesons, appears to come to rest and to lead to the emission of a particle of smaller mass, which, at the end of its range, produces a nuclear disintegration. The ranges of the secondary particles, in the three cases, are 20, 25 and 45 μ , respectively. The authors were not aware of our results when they suggested to us that their observations may correspond to the spontaneous decay of heavy mesons. According to their description, these events are precisely similar to those we should expect to observe in C2 emulsions as a result of the spontaneous decay of heavy particles of the type we have postulated; for any particles of low specific ionization will not be recorded by the Ilford plates. The observations of Peters and Bradt appear, therefore, to give further support for the assumption that the present observations are not due to a chance juxtaposition of tracks; and they suggest that it will be possible, in the near future, to find similar examples suitable for making a detailed analysis.

¹ Berriman, *Nature*, **162**, 992 (1948).

² Leprince-Ringuet, *C.R.*, **226**, 1897 (1948). Rochester and Butler, *Nature*, **160**, 855 (1947). Bradt and Peters, Report to the Bristol Symposium, 1948 (in the press). Alchanian, Alchanov and Weissenberg, *J. Exp. and Theoret. Phys., U.S.S.R.*, **18**, 301 (1948); and other references.

³ Camerini, Muirhead, Powell and Ritson, *Nature*, **162**, 433 (1948).

⁴ Goldschmidt-Clermont, King, Muirhead and Ritson, *Proc. Phys. Soc.*, **61**, 138 (1948).

⁵ Lattes, Occhialini and Powell, *Proc. Phys. Soc.*, **61**, 173 (1948).

⁶ Serber, Report of Solvay Conference for 1948.

⁷ Dilworth, Occhialini and Payne, *Nature*, **162**, 102 (1948).

⁸ Occhialini and Powell, *Nature*, **162**, 168 (1948).

⁹ Halpern and Hall, *Phys. Rev.*, **73**, 477 (1948).

¹⁰ Livingston and Bethe, *Rev. Mod. Phys.*, **9**, 263 (1937).

¹¹ Camerini and Lattes (private communication); see also Powell and Occhialini, "Nuclear Physics in Photographs", 112 (Oxford, 1947).

DEVELOPMENT OF LEATHER CHEMISTRY

THE first applications of scientific knowledge to the problems of leather manufacture may be said to have been made about 1890, and the initiation in the following year at the Yorkshire College (now University of Leeds) of a course of lectures devoted to the subject was an indication that a new field of technology had gained recognition. Five years later, through the foresight and generosity of local tanners and the Worshipful Company of Skinners, a special department was built to house the new subject, and H. R. Procter was appointed to fill the newly created chair in 1898.

The industry, which was being encouraged to examine its methods along scientific lines, was one dating from primitive times, and little advance had been made in methods of manufacture or in the principles underlying them since their inception. Moreover, and perhaps because of this, the industry as a whole was a conservative one, and early workers in the field had to contend with a rooted distrust of new ideas which took a long time to break down. It was without doubt fortunate for the future development of the subject that the man chosen to hold a key position at the outset was Procter, who deservedly earned the title of 'father of leather chemistry'. Working in a more leisurely age than the present, he did not publish his well-known theory of protein swelling until 1916; but during the intervening years he was laying the foundations firmly by his influence on the succession of students who passed through his hands, as well as by his own published work. Largely by reason of his efforts, the industry was of a sufficiently scientific turn of mind by 1920 to support the foundation of the British Leather Manufacturers Research Association, which is one of the oldest associations of its kind in Great Britain. The growth of knowledge in this field, and the amount of work which has been done, may be appreciated by a perusal of three publications issued to commemorate the twenty-fifth anniversary of this Association*, which is, in effect, a summary of almost all important investigations relating to leather carried out during the period throughout the world.

Since the materials used in leather manufacture are of many different types, both organic and inorganic, and as the processes employed involve to some extent the application of almost all branches of chemical knowledge, there can be few other industries in which the research worker must be familiar with so many different aspects of chemistry. Many problems have been elucidated by virtue of investigations in other subjects, probably the most fruitful contributions coming from biochemists, especially those working on proteins, as a result of which the composition and structure of the tanner's most important raw material, collagen, is more or less settled. From the realm of organic chemistry have come numerous studies on the constitution of the tannins which, from Fischer's early synthesis of penta-*m*-digalloyl- β -glucose and from Freudenberg's work on the condensed tannins to the work of present day, have materially contributed to the understanding of vegetable tanning. Information on these matters is, however, by no means complete, and recent research, especially on the important tannin constituent of mimosa bark, has directed the attention of leather chemists in particular to the importance of this line of investigation.

In this branch of their subject, as in many others, leather chemists have in many cases made notable contributions not only to the understanding of their own problems but also to chemical knowledge in general. It may not be widely known that Procter's work on the swelling of gelatine was promoted by the observation of swelling phenomena in hides during operations prior to tanning; and the discovery that chromium salts were valuable tanning agents led to a large amount of research on the properties of their solutions, with results of wide interest.

* Progress in Leather Science, 1920-1945. Vols. 1, 2, 3. Pp. xvi + 705. (London: British Leather Manufacturers Research Association, 1946-48.)

Much of the fundamental work on tannery processes has been concerned with the mechanism of tannin-collagen combination, although tanning itself is only one of a large number of operations involved in the manufacture of leather. Several general lines of attack on the problem have yielded valuable information, no matter which type of tanning agent, organic or mineral, has been under examination. The introduction in 1934 of the shrinkage temperature as a measure of the thermal stability of collagen has been used not only as an indication of the increase in cross-bonding between adjacent polypeptide chains which occurs in some types of tanning but also as a means of clarifying protein structure; and some of the latest published work of Jordan Lloyd, who was director of the British Leather Manufacturers Research Association from 1927 until her death in 1946, was concerned with the shrinkage temperature of collagen in organic solvents. Modifications of the reactive groups in collagen by de-amination to remove the lysine amino group, removal of the guanidine group of arginine by Sakaguchi's method, combination with formaldehyde, and methylation, have all been carried out; and the effect has been considered on such properties as combination with acids, bases and tanning agents. Similarly, the influence of modification by tanning on the acid- and base-combining capacity of collagen, and the effect of combination with one type of tanning agent on its behaviour to another contrasted type, have been widely studied. The role of hydrogen ion concentration in manufacture is now well understood, and has been interpreted in conformity with the zwitterion theory of protein structure.

The vegetable tanning process presents a number of questions which have not been answered; and several theories on the mode of combination of tannin and collagen have been proposed, ranging from an adsorption mechanism to salt formation involving the amino groups of the protein molecule. The concept of hydrogen bonds has been invoked to explain not only tannin-collagen combination, but also the relatively large amount of tannin fixed in leather; and it is thought that tannin is bound to tannin by means of hydrogen bonds, and that only about half the tannin shown by analysis to be 'fixed' is actually attached to the protein. In fact, all types of chemical bonds play a part in the process to an extent depending on the constitution of the tannins present, external conditions in the tan liquors, such as pH and other factors; and it would be impossible to distinguish the extent of each in any given sample of leather. More important from the tanner's point of view is the fact that much knowledge has been gained about the functions of the non-tannin constituents of the liquors with which he makes sole leather, especially the large number of acids and salts present, which have a profound effect on the quality of the leather produced. In this case, the problem has largely been one of analytical procedure and has been partly solved by the use of ion-exchange resins, combined with the examination of the titration curves of the liquors; but recently the method has been subjected to some criticism.

The chrome-tanning process has proved no less intractable than that using vegetable tannins. It was not until some insight had been gained into the chemistry of chromium salts that any successful attempt could be made to enunciate a theory which would explain the phenomena accompanying chrome-

leather manufacture, although the conditions necessary for successful tannage were known long before the reasons for them, especially the importance of the acidity of the bath. The application of Werner's co-ordination theory has proved of enormous value in explaining the course of the reaction, and most theories assume the co-ordination of the chromium complex with some part of the collagen molecule. The increase in pH necessary to obtain combination between collagen and the chromium compound affects both the complex itself and the protein, and co-ordination could occur between an ionized carboxyl group and the complex. It seems very likely that combination takes place between adjacent polypeptide chains through the complexes, and this is one explanation of the high degree of stability of chrome-tanned leather towards boiling water. Attempts to explain chrome-tannage on the basis of salt formation have not been so successful, except in cases where anionic complexes are present in the tanning bath.

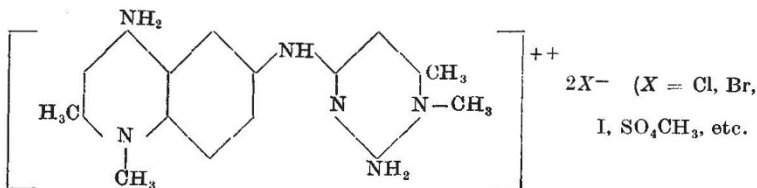
What might be referred to as less important methods of tanning have not received as much attention, except in the case of formaldehyde, which is linked to the wider problem of the protein-formaldehyde reaction. Quinone tannage, although of no commercial importance at present, has nevertheless been investigated for the light it throws on the vegetable tanning process.

Many operations other than tanning have been investigated by leather chemists; but space allows mention of only a few. The liming process for the removal of hair, especially the function of unhairing agents in accelerating the reaction, has been explained in the light of a great deal of work carried out on wool, while the effect of the same operation on collagen has been shown to involve mainly the amide groups and possibly the arginine. The most important modification which collagen undergoes in liming is in the alteration of the fibre structure due to plumping, and in the separation of the fibre bundles into fibrils.

Some of the most valuable work carried out, particularly by the British Leather Manufacturers Research Association, has been in the development of microscopic examination as a guide to the quality of leather, and the large number of photographs in the publications referred to bears testimony to the extent to which this method has been adopted. In the field of physical testing, methods have been introduced for the determination of permeability of leather to water and water vapour, resistance to abrasion and allied phenomena, all of which, with certain reservations, give a more immediate and practical indication of quality in use than the older method of chemical analysis. A great deal of less spectacular work has enabled tanners to overcome faults derogatory to the value of their products, such as stains resulting from bacterial action in the curing of the raw hides, various exudations known under the term 'spues', liability of some leathers to rot in acid atmospheres and many other similar defects. These operational problems have been the cause of a large amount of work in Great Britain and the United States for a number of years; but it is true to say that the resistance of vegetable-tanned leathers to acid deterioration especially has been markedly increased.

It has been possible in a short space to indicate briefly no more than a few of the advances made during the last quarter of a century. The chief contributions to the problems involved have been made

by chemists in Great Britain, on the continent of Europe, and in the United States, where an Association of Leather Chemists was formed in the early years of this century. Many papers have been published from laboratories of industrial organisations and private firms, which alone shows how far the industry has moved since Procter's early days. In the last decade or so, schools of tanning with attendant research organisations have grown up in South Africa, Australia and New Zealand. While the field has been expanding rapidly, no leather chemist can claim that more than a fraction of the problems which face him has been settled, and it becomes more apparent yearly that most of the operations with which he deals are far more complicated than had been realized. In regard to fundamental problems, the past twenty-five years have seen a notable clearing of the ground. In the realm of manufacture, it is probable that in the future much more attention will be paid to the use of synthetic agents for many tannery processes as replacements for time-honoured natural materials, which for one reason or another are becoming less easily available each year.



These salts, which have the accompanying formula, will be referred to for convenience as 'Antrycide' salts.

We give in Table 1 a brief summary of the experimental findings obtained with one of these salts in the treatment of various trypanosome infections in mice; in all experiments the drug was administered subcutaneously.

Against a *Trypanosoma congolense* infection, a single dose of 1 mgm. of 'Antrycide' chloride per kilo body-weight was curative. Half this dose effected a proportion of cures. Similarly, activity was shown by this compound against many other experimental trypanosome infections, for example, against those due to *T. rhodesiense*, *T. brucei*, *T. evansi* (India), *T. evansi* (Sudan), *T. equiperdum* and *T. equinum*. Susceptibility to the drug of the different trypanosome species was not uniform throughout the series, but by adjustment of the dose, cures could be obtained in every case. We did not encounter marked toxic effects even with doses many times those necessary for cure.

It should be noted that the figures in Table 1 relate to particular strains of the trypanosome species indicated. Some variation was experienced with certain other strains; for example, one strain of *T. congolense*, isolated in Kenya, showed marked resistance compared with the Busimbi strain, and a dose of about 2.5 mgm./kgm. was required to produce consistent cures in mice.

'Antrycide' salts also possess marked prophylactic action against experimental trypanosome infections. Mice, rats and rabbits were first treated with the drug, and then after a varying period of time were 'challenged' with trypanosomes. It was found that, with suitable doses, the animals could be protected against infection for some weeks. The results of some typical experiments with *T. congolense* (Busimbi strain) in mice are recorded in Table 2. If no try-

'ANTRYCIDE': A NEW TRYPANOCIDAL DRUG

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THE discovery of a new drug, 'Antrycide', showing great promise in comprehensive field trials as a trypanocide, has already been referred to in an announcement from the Colonial Office. This new drug resulted from a systematic study of the chemotherapy of trypanosomiasis in these Laboratories, and although a full account of our researches must

Table 1. Trypanocidal action of 'Antrycide' chloride against various *Trypanosoma* species

Dose (mgm./kgm.)	<i>T. rhodesiense</i> (Tinde)	<i>T. brucei</i> (Liverpool)	<i>T. congolense</i> (Busimbi)	<i>T. evansi</i> (India)	<i>T. evansi</i> (Sudan)	<i>T. equiperdum</i>	<i>T. equinum</i>
25	C						
12.5	C						
5	C	C and R					
2.5		R					
1.25			C	C	C and R	C	C
1.0			C				
0.5			C and R	C and R	R	C	C and R
0.25			R			C and R	
0.125			R and DD				

C = Cure: blood freed from trypanosomes for 28 days. R = Relapse: blood freed from trypanosomes temporarily, appearing again within 28 days. DD = Delayed death: blood not freed from trypanosomes

await later publication, a few preliminary observations may be of interest.

After considerable chemical exploration, 4-amino-6-(2'-amino-6'-methylpyrimidyl-4'-amino) quinaldine-1:1'-dimetho salts were found to possess outstanding trypanocidal properties against laboratory infections.

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panosomes were to be found in the blood 28 days after challenging, then the animals were regarded as completely protected (P in Table 2). Incomplete protection (I) was judged by delayed death as compared with untreated control animals or by the appearance of trypanosomes in the blood of the test animal before completion of the experiment.