Institution: University of Northampton

Unit of Assessment: 12 - Aeronautical, Mechanical, Chemical and Manufacturing Engineering

Title of case study: Link-Lock theory of collagen stabilisation

1. Summary of the impact

The leather industry is globally significant: the supply chain, from leather production to leather goods manufacture is currently worth in the order of $1 trillion per annum. Although written records show that leather production is at least 5,000 years old, an understanding of the chemical principles underpinning the reactions involved only began at the turn of the 19th century, roughly corresponding to the development of modern chemistry and, coincidentally, with the revolutionary introduction of chrome tanning. At that time, the basis of the stabilising reaction was assumed to be crosslinking, whereby the component strands of protein are linked like stitches by the tanning chemical and this was the accepted view thereafter. Furthermore, it was also accepted that the ability of tanning reactions to confer high hydrothermal stability is a property of a few unrelated chemistries, of which chromium(III) tanning is the best known example.

Link-lock theory is revolutionary, insofar as it is the first new thinking in the chemical stabilisation of collagen in over half a century. This view of tanning was the outcome of examining the reaction with modern analytical instrumentation and applying a weight of evidence from the literature. The consequence has been the rejection of the accepted view of tanning mechanism, in favour of a simpler but more powerful theory. The principles of the theory can explain the effects of all known tanning processes. In an applied technology, its use is most powerful as it can predict the outcome of all, even as yet unknown reactions. Moreover, it is a major part of the way in which practitioners can predict details of the processes required to make leather and other biomaterials with desired properties and performance.

The fundamental importance of the theory is that it allows the subject to move on as it is more powerful than the alternative view and there is much evidence to support it. By combining this thinking with other new thinking into wider aspects of the heterogeneous chemistry, modifying collagen is now placed on a firm basis of leather science, which means that the outcomes of reactions can be predictable. The primary impact of this new view of protein stabilisation lies in the ways in which the thinking has and is informing developments of collagenic biomaterials and applications in the global leather and associated industries.

2. Underpinning research (indicative maximum 500 words)

The 'link-lock' theory was developed by Covington, (who was Professor, and then in October 2011 became Emeritus Professor of Leather Science), over a period of about 10 years [1,2]. Here, the most important experimental collaboration was with the Universities of Canterbury and Manchester, when X-ray studies were undertaken on the synchrotron at Daresbury [3]. This was the first time the chrome tanning reaction had been subjected to examination at the molecular level. Although it had been expected that the observations on collagen tanned with basic chromium(III) sulfate would confirm the prevalent view of crosslinking, unexpectedly, the direct evidence contradicted it as follows:

(i) bound chromium is in the form of a linear tetramer, not a dimer.

(ii) sulfate is not bound to chromium species as a ligand – it functions as a stabilising component of the reaction i.e. the chrome tanning reaction has a combination mechanism.

(iii) if the chrome tanning reaction is dependent on the crosslinking mechanism, the outcome would be independent of the anion: however, the tanning reaction is highly dependent on the anion e.g. tanning with chromium(III) chloride or perchlorate can only yield shrinkage temperature no higher than 85^{o}C, like any other single tanning species.

The latter observation means that chrome tanning falls into line with other known reactions capable of conferring high hydrothermal stability, but are characterised as combination processes e.g. plant hydrolysable polyphenol + aluminium(III) salt.

Therefore, all tanning reactions, regardless of the chemical nature of the tanning agents and the way they react with collagen, are fundamentally the same, insofar as they merely physically interfere with the shrinking mechanism when collagen is heated in water. Consequently, any single reagent is only capable of raising the observed denaturation temperature from 65 to no more

than 85°C: this is referred to as the linking reaction. If a second reagent is applied, it can react on the collagen and interact with the first reagent in one of three ways: independently, antagonistically or synergistically. In the latter case, the reaction is designated the locking reaction, because it locks the molecules of the first reaction together: in this way, a new tanning system is created, a matrix or scaffolding, which stabilises the collagen by concerted interactions/bonds. The consequence of this process is that, when the modified collagen is subjected to wet heat, it is much more difficult for the triple helix structure of collagen to unravel and for the random coils of the denatured protein to collapse into the interstices of the highly organised collagen structure: this is observed as a marked raising of the shrinkage temperature, up to 130°C [4].
The theory incorporates a new understanding of the chrome tanning reaction: more importantly, this understanding provides the basis for making improvements not only in the properties and performance of chrome tanned leather but also to the environmental impact of its production [5, 6].

3. References to the research (indicative maximum of six references)

1. Covington, A.D., "New tannages for the new millennium", .J. Amer. Leather Chem. Assoc., 1998, 93(6), 168.
2. Covington, A.D., "Theory and mechanism of tanning: current thinking and future implications"J. Soc. Leather Technol. Chem., 2001, 85(1), 24.
3. Covington, A.D., Lampard, G.S., Menderes, O., Chadwick, A.V., Rafeletos, G., O'Brien, P., "Leather tanning studies using Extended X-ray Absorption Fine Structure (EXAFS)" Polyhedron", 2001, 20, 461.
4. Covington, A.D., Song, L., Suparno, O., Koon, H.E.C., Collins, M.J., "Link-lock: an explanation of the chemical stabilisation of collagen", J. Soc. Leather Technol. Chem., 2008, 92(1), 1.
5. Covington, A.D., "The mechanism of chrome tanning", Global J. Inorg. Chem., 2010, 1(2), 119.
6. Covington, A.D., "Prediction in Leather Processing: A Dark Art or a Clear Possibility", J. Soc. Leather Technol. Chem., 2011, 95(6), 231.

For reference 3, Lampard's doctoral studies were funded by the University of Northampton, Menderes' doctoral studies were funded by the Turkish Government, Professor Chadwick and Mr. Rafeletos were collaborators from the University of Canterbury, Professor O'Brien was a collaborator from the University of Manchester.
For Reference 4, Song's doctoral studies were funded by the University of Northampton, in a collaborative programme with Sichuan Union University of Chengdu, P.R. China and Suparno's doctoral studies were funded by the Indonesian Government. Professor Collins and Ms. Koon were collaborators from the University of York.

4. Details of the impact (indicative maximum 750 words)

Technological progress and acceptance of new thinking in the leather industry is conservatively slow, but the link-lock theory appears to have been embraced surprisingly quickly. Since the first publication of the link-lock theory in the technical leather literature in 2008, the theory was refined for further dissemination in the technical magazine World Leather, Oct/Nov 2010. The theory was used extensively in the argument for predicting the processing by which desired characteristics could be conferred to leather, published in the Journal of the Society of Leather Technologists and Chemists, 2011, 95(6), 231, taken from the Procter Memorial Lecture given to the Annual Conference of the Society of Leather Technologists and Chemists of UK in 2010, and presented to the International Union of Leather Technologists and Chemists Societies Congress in Valencia, Spain in 2011, a biennial meeting of the technical arm of the global leather industry.
The theory was extensively treated in the following book, the first treatment of leather science since 1993, in which the future of tanning was reviewed in the light of the new thinking: Covington, A.D., *Tanning Chemistry. The Science of Leather*, Royal Society of Chemistry Publishing, Cambridge, 2009 (ISBN:978-0-85404-170-1)
The link-lock theory, however, has been disseminated beyond academia into the global leather and associated industries: it is known to be being used in the thinking of leather scientists in the USA and Europe. In particular, The American Leather Chemists Association (ALCA) gave Covington the Alsop Award in 2011 for '*outstanding scientific or technological contribution to the leather industry*'. It should be noted that ALCA were founded in 1903 specifically to promote the advancement of

science and engineering in their application to the leather and leather product industries.
In practical terms, the link–lock theory is informing the development programme of the Lanxess company of Germany. They are currently marketing a new tanning agent based on poly (carbamoyl) sulfonate, In order to optimise the effect of the reagent in the market, the link-lock theory is being used to define how the technology can be extended in terms of combinations of other chemicals with the base reagent. In this way, a new generation of tanning processes can be devised, allowing tanners an organic option to the global standard of chrome tanning and a means to avoid the environmental difficulties of using metal chemistry (contact Dr. Dietrich Tegtmeyer, Lanxess).
Link-lock is also the basis of the thinking in trying to define the development of a new generation of tanning chemicals being undertaken by Buckman International, an American based chemical supply house for whom Covington acted as Consultant in 2011. Since there is a developing market for leather which is chromium free, they like other supply houses are interested in supplying alternative tanning reagents to the tanning industry. Here, the particular interest lies in organic alternatives to chromium(III) chemistry and any successful alternative must match as many of the properties of chrome tanned leather as possible. The only way to achieve high hydrothermal stability, required in modern applications of leather, is to use the principles of link-lock (contact Mr. Elton Hurlow, Buckman).
The ECCO company, a multinational leather business based in The Netherlands, Indonesia and P.R. of China, currently sends cohorts (ca.10 pa) of its brightest technologists to the University of Northampton for the MSc in Leather Technology. The purpose is to educate them in the latest thinking, in which link-lock theory and associated developments are central. Graduates return to their factories equipped with the ability to engage in development programmes to make operations more profitable: this is the return on the investment made by the parent company (contact Mr. Arthur Jones, ECCO).

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Brown, E.M., Dudley, R.L., “Approach to a tanning mechanism; study of the interaction of aluminium sulfate with collagen”, J. Amer. Leather Chem. Assoc., 2005, 100(10), 401.
2. Reich, G., “From collagen to leather – the theoretical background”, BASF Ludvigshafen Germany, 2007.
3. Tegtmeyer, D., Tysoe, C., Reiners, J., “X-Tan an innovative organic tanning technology with superior sustainability”, Proc., IULTCS Congress, Valencia Spain, September 2011.

Reference 1 states: *‘Recent proposals ... that tanning is a matter of protein modification, not just collagen crosslinking, are supported by our recent finding that hydrothermal stability of leather is a function of total bound chromium, not just a fraction that forms ‘productive crosslinks’.*’
Reference 2 is a privately published monograph written by one of the world’s foremost leather scientists in the latter part of the last century, in which he discusses aspects of the thinking leading to the link-lock theory – although this work was in preparation just before the term was coined. Reich accepts the developing conclusions relating to the importance of the matrix created by the tanning system in stabilising the protein.
Reference 3 Is the text corresponding to the oral presentation at the Congress of the International Union of Leather Technologists and Chemists Societies, given by Tegtmeyer of the company Lanxess, an international chemical supply house, during which much mention was made of analysing the mechanism and performance of the new tanning system by the link-lock theory.

Beneficiaries who could be contacted to corroborate the claims made.

Vice President, Head of Product Development and Application, Lanxess Deutschland GmbH, Germany
Gobal Market Development Manager, Buckman Laboratories International, Inc., USA
ECCO Leather Academy Director, ECCO Tannery (Thailand) Co. Ltd., Thailand