Development of CHED Fungicide for the Leather Industry*

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INTRODUCTION

The transformation of hides and skins into leather renders triple helical collagen resistant to proteolytic attack by spoilage microorganisms. In fact, this property is considered by some leading leather scientists as the one strict definition of tanning[1]. The rapid growth of fungi on moist tanned leathers is not contradictory to this definition, as recent work has confirmed that the main source of nutrition for fungi growing on the surface of leather is not the collagen fiber, but the fat and grease[2] present in the leather. Fatty materials are necessary for fiber lubrication, but are also an excellent nutrient and energy source for fungi. Sufficient moisture and the acidity of leather further favor fungal growth.

Knowing these facts is little consolation to the leather industry that suffers losses running into the tens of millions of dollars each year because of fungal growth problems. These problems occur despite attentive addition of fungicide chemicals during processing. When such failure occurs the main reasons are inadequate amount of fungicide added, improper fungicide selection, incompatible processing environment, and poor leather handling, packaging or storage conditions. Exposure to fungal spores occurs when leather is open to the environment. Warmer temperatures and high humidity levels will further support growth. Moist leathers will grow mould rapidly with resulting discoloration, staining, and physico-chemical changes that can significantly decrease the value of leathers or leather articles. Indirect losses related to management time, rework, logistical issues, and upset customers add to the financial loss. Fungicide products are typically among the more expensive chemicals used by the tanner, but this price compares favorably against the cost of even a single outbreak of mold.

Fungi belong to a very large and diverse kingdom of living organisms. The majority of fungi are microscopic – invisible to the naked eye. When we do see mould growing on leather, it is typically a colony of tens- or even hundreds- of thousands of organisms. Under the microscope, their morphology resembles that of plants, but genetically and biochemically they have many characteristics that more closely link them to the animal kingdom. This genetic similarity provides some insight as to why fungicides are potentially hazardous for animals, including humans, and the environment. This is why fungicides should be used with appropriate precautions to ensure no harm occurs during or after use. In regulated countries, government authorities strictly control which products may or may not be used. The expense and potential harmful nature of fungicides is strong motivation to ensure safe and optimal use of these types of products.

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*Based on a paper presented October 2012 at FLAQTIC Congress in Uruguay.

[1] Covington, Anthony D.; Tanning Chemistry – The Science of Leather, The Royal Society of Chemistry, UK, pg 195, 2009.

[2] Zugno L, Hurlow E, Oppong D; Fungal Growth on Wetblue, JALCA, 105, pg 1-7, 2009.

FUNGICIDES FOR LEATHER INDUSTRY USE

There are surprisingly few active substances that are used in the leather industry for fungal control. Few chemical compounds can withstand the harsh industrial processes involved in leather making as well as the difficult performance requirements demanded of fungicide products. The compounds must of course also not appear on restricted substances lists. It is the authors' estimate that more than 95% of leather today is preserved by one or more of only four active substances (see Table 1). TCMTB may be used successfully on its own. The other compounds listed are typically either applied in combination with TCMTB or another active substance if long-term preservation is required.

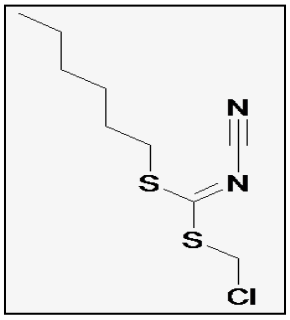
Table 1: Fungicide active substances in common use in the leather industry worldwide

Fungicide	CAS	Common Name(s)
2-(Thiocyanatomethylthio)benzothiazole	21564-17-0	TCMTB
2-Octyl-4-Isothiazolin-3-One	26530-20-1	OIT (ITZ)
ortho-Phenylphenol	90-43-7	OPP
p-Chloro-m-cresol	59-50-7	PCMC (CMK)

The existing chemicals have been reviewed and approved by regulatory authorities in countries that have strict regulatory requirements in place. If used responsibly, these chemistries can be applied without undue concern for damage to the environment, or danger to industry workers or the consumer. The listed compounds have all been around for many years and there have been calls for "greener" replacements. To be responsible, such calls should be considered carefully. The selection is already limited and we are not aware of many potential successors coming through the pipeline. It should also be noted that the lack of new chemistries is in part due to the relatively small size of the leather industry. It is very expensive to get fungicides approved by regulatory agencies and it takes a long time to complete the required testing. For example, estimates are around $5 million and 5 years to register a new active substance in the European Union or the USA today.

Despite this background, an encouraging new chemistry has been developed for leather and is now available for the industry. This new molecule, called CHED (S-Hexyl-S'-chloromethyl-cyanodithiocarbimate), is structurally depicted in Figure 1. Buckman scientists conducted a systematic study of the asymmetric substitution of carbimates which were known by the researchers to exhibit antifungal activity. They found that the hexyl derivative exhibited the lowest MIC value (Minimum Inhibitory Concentration) and the molecule performed very well against standard active substances used by the industry. Research into synergy properties was also very positive, resulting in the development of highly effective products based on formulations containing multiple active substances.

Figure 1: Structure of CHED



A composition patent[3] was issued in 2007 and in 2010 a synergy patent[4] was granted for performance of the chemical on its own and in combination with known active substances. The initial development of CHED products and results of laboratory testing has been previously reported[5]. Products containing CHED have now been selectively introduced to the industry for long-term performance testing under tannery production conditions.

PERFORMANCE EVALUATION METHODS

To evaluate the long-term preservation of leather materials against potential attack by fungal organisms is not easy. This is because the presence of fungal spores is ubiquitous and growth of these microscopic organisms is complex. These are living things and growth is dynamic. Laboratory methods allow one to carefully control parameters, such as microorganism species, level of inoculation, nutrients, substrates, temperature and humidity, but no single test will mimic all real world situations. Within a tannery the prevailing environment and process conditions are always in flux. The problem of evaluating performance is best solved by running a series of standard tests and then estimating real world performance based on subjective experience.

Extraction Analysis (EA) indicates how much of the active substance is present in a sample and this method can be used to determine how well the active substance is taken up by the leather. To understand extraction numbers and especially to compare between leathers of different origin, it is important to normalize the results to standard thickness and moisture content. Fungal growth is a surface phenomenon and correction to standard thickness is helpful.

The leather industry has adapted various challenge tests for evaluating the resistance of wet leathers to growth of fungi. Some versions involve exposing the leather sample to growth of fungi in an agar plate. Although this method is fairly repeatable in the laboratory, there are technical problems with interpretation of results. The use of an Environmental Chamber (EC) to expose the leather samples to fungal spores under optimal growth conditions and then

[3] Fenyes J. et al; "Fungicidal compositions and methods using cyanodithiocabimates"; USPTO 7,157,017, 2007

[4] Bryant S.; "Microbicidal compositions including a cyanodithiocabimate and a second microbicide"; USPTO 7,772,156, 2010.

[5] Bryant S., Hurlow E., Whittemore M.; "A new Antifungal Agent for the Leather Industry", JSLTC, Vol. 95, pg 7-10, 2011; *and* presented at the VIII AICLST in Kolkata, Nov 2010.

evaluating leather performance, yields best correlation with real-world observations. This method is called a Tropical Chamber (TC) test when run at elevated temperature.

Additional tests are sometimes used in product development and troubleshooting, but the abovementioned methods are the best predictors of real-world performance and widely used by Buckman in monitoring fungal control programs for the leather industry worldwide.

CASE STUDIES OF CHED BASED PRODUCTS

Extensive production trials over a period of more than 2 years have now been completed in tanneries around the world. Case Study results are shown below and in Table 2 using a synergistic combination of three active substances including CHED[6]. These results are from standard production runs using different raw materials, processing equipment, recipes. The types of wetblue that are the subject of these case studies are for different end uses.

Case Study 1: A large tannery situated in a warm climate produces full thickness wetblue from fresh hides for domestic and export markets. Expectations of preservation for a minimum of 6 months were met with a standard dosage of 0.16%. In real life, some of this wetblue was stored for well over 1 year with continued good preservation.

Case Study 2: The second example is a medium size tannery that produces wetblue for export from fresh bovine hides. The wetblue produced has slightly lower averages for extracted active substance than the first tannery example with the same fungicide dosage. Different raw materials, process equipment, recipes and process conditions may account for variation in extracted active substance. Likewise, differences in base weight calculation (e.g. limed pelt weight or transfer weight) that is used to calculate the dosage typically varies between tanneries and can also contribute. Challenge testing indicated acceptable fungal protection.

Case Study 3: The third example is another large tannery that processes fresh hides to wetblue for export. It is necessary to optimize dosage at each tannery based on performance requirements and results of both extraction analysis and challenge testing. In practice, optimization of the dosage requires extensive field trials and a lot of practical testing and measurement. In this instance, a reduced dosage resulted in good extraction values as well as excellent challenge testing results.

Table 2: Normalized extraction data (ppm) and Environmental Chamber performance

Case Study	Sample Size (n)	Dosage %	Normalized Extraction Values (EA)			TC @ 4 weeks
			Active A	Active B	Active C	
1	301	0.16	45	28	22	10 / 10
2	126	0.16	33	23	15	10 / 10
3	19	0.14	45	40	18	10 / 10

It should be noted that there typically is significant variation in the extraction numbers between individual samples from the same tannery as well as between tanneries. Considering this variability, special care must be given to using a suitable sample size to draw valid conclusions. The high performance of CHED along with measured synergy allows significantly reduced

[6] Busan® 7555 from Buckman

amounts of individual and total active substances to be present in the leather as shown by these three tannery examples. As fungicides are potentially harmful for humans and the environment the reduced amount of potentially harmful chemical substances has both commercial and ecological benefit.

CONCLUSIONS:

The discovery and development of a new highly effective fungicide for the leather industry that works well with existing products and on its own to meet industry performance requirements is not a common event. Development of CHED from initial research phase, through development of stable formulations, laboratory scale testing, optimization of manufacturing, and on to industrial scale testing represents a major commitment of time and resources.

This paper shares data from more than two years of tannery production experience using CHED in synergistic combination with known actives. Performance results for CHED based products compared to the leather industry standard, i.e. a 30% formulation of TCMTB, show excellent results at lower dosage levels. Residual active substance levels in the leathers are much lower than any other fungicides available in the market today. CHED provides the tanner with an option that meets requirements for low residual levels of active substance without compromising long-term preservation, in line with recognized sustainability objectives.

NOTES & ACKNOWLEDGEMENTS:

Buckman is currently the only listed participant who is registering TCMTB under the European Union Biocidal Products Regulation (BPR, EU 528/2012) and Buckman is in the process of registering CHED under the transitional measures of this regulation to ensure continued availability of both CHED and TCMTB for the global leather industry. The authors acknowledge the work of many dedicated Buckman associates who have been involved in running production scale trials to introduce the product Busan® 7555; and those involved in the analytical testing of many hundreds of leather samples around the world. Large scale trials are now underway on a “stand-alone” CHED product called Busan® 7658.