The influence of occupational exposure to sulphuric acid mist on skin barrier function in a base metal refinery

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Mini-dissertation submitted in partial fulfillment of the requirements for the degree *Magister Scientiae* in Occupational Hygiene at the Potchefstroom Campus of the North-West University

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It all starts here ™

Preface

This mini-dissertation is presented for the partial fulfilment of the degree *Master of Science in Occupational Hygiene* at the School of Physiology, Nutrition and Consumer Sciences of the North-West University, Potchefstroom Campus. The article format was used for the purpose of this study. References are presented according to the guidelines of the *Annals of Occupational Hygiene*. Chapter 3 is written in the form of an article. Relevant literature is discussed in Chapter 3; Chapter 2 serves as a literature study, providing the reader with a more in-depth understanding of the literature background. Chapter 4 is the final chapter, and provides a summary of the results obtained in the study; all discernible factors are discussed after which conclusions are drawn. Recommendations were made in order to improve conditions in similar areas as to where this study was conducted, seeing as though employee health is involved.

Author's contribution

This study was planned and executed by a team of researchers. The contribution of each is reflected in Table 1.

Table 1: Research Team

Name	Contribution
Mr NC Meyer	Literature research, statistical analyses and writing of the mini-dissertation including the article.
Mr PJ Laubscher	Reviewing of the mini-dissertation and administration associated with the research project.
Mr CJ van der Merwe	Reviewing of the mini-dissertation.
Mr M Schoonhoven	Assisted with the planning and financial administration of the study.

The following is a statement from the co-authors regarding the role they played in the study:

I declare that I have approved the mini-dissertation and article and that my contribution as reflected in the above table is a true reflection of my actual contribution and that I hereby give my informed consent that it may be published as part of NC Meyer's M.Sc. (Occupational Hygiene) mini-dissertation.

Mr PJ Laubscher   Mr CJ van der Merwe   Mr M Schoonhoven

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Table of Contents **Page**

List of tables .... Page

Author's contributions

Chapter 3

List of figures **Page**

Chapter 2

Chapter 3

List of abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists, USA
a.u.	arbitrary units
$CuCl_2$	copper chloride
$CuSO_4$	copper sulphate
$g/m^2/h$	gram per square meter per hour
H_2SO_4	sulphuric acid
l/min	litre per minute
mg/m^3	milligram per cubic metre
$NiCl_2$	nickel chloride
NiSO4	nickel sulphate
NIOSH	National Institute for Occupational Health and Safety
NMF	natural moisturising factor
OEL	occupational exposure limit
pH	measure of acidity or alkalinity
P_{ow}	octanol-water partition coefficient
PPE	personal protective equipment
SLS	sodium lauryl sulphate
TEWL	transepidermal water loss
TLV	Threshold limit value
TWA	time weighted average

Summary

Title: The influence of occupational exposure to sulphuric acid mist on skin barrier function in a base metal refinery.

Motivation: The skin is the primary barrier between the internal and external environment. Damage to this barrier will lead to adverse health effects such as water loss through the skin as well as the absorption of exogenous and potentially hazardous substances. The monitoring of employees' skin condition is not yet seen as feasible in the field of Occupational Hygiene, this study should shed some light on its importance.

Aim: To determine the extent of the possible negative influence of sulphuric acid mist on the skin condition and skin barrier function of employees working at a base metal refinery, by assessing the concentrations of sulphuric acid mist in the air and correlating it to three skin variables. These three variables are transepidermal water loss (TEWL), hydration of the skin and skin surface pH. Consequently the correlation between pH and TEWL, pH and hydration and TEWL and hydration, will also be investigated.

Methodology: The concentration of sulphuric acid mist present in the air of the copper- and nickel tank houses was measured using NIOSH method 7903 for inorganic acids. Measurements of the skin barrier function were also done to determine the state of the skin condition at that time. Three variables were measured, namely TEWL, stratum corneum hydration and skin surface pH. The sulphuric acid mist concentrations were then correlated with the skin values to determine the influence of sulphuric acid mist on the skin barrier function. Qualitative swab samples were taken on the test subjects to determine if copper or nickel was present on the skin or not. This was done for two reasons: Firstly, if copper or nickel is present on the skin, these metals could have been absorbed into the skin and contributed to the skin being damaged. Secondly, if the skin variables show that skin damage has occurred on these workers, there might be higher possibility that these metals will be absorbed through the skin which could have adverse health effects.

Results and conclusions: The results of this study indicated that the palm of hand and back of hand areas showed high TEWL values and low hydration values. This is to be expected as these areas are subjected to mechanical friction by PPE leading to wear and tear on the skin surface. Few meaningful correlations could be drawn between the sulphuric acid mist concentrations encountered in the tank houses and the three measured skin variables. It is therefore concluded that the low level of sulphuric acid mist in the atmosphere had no detectable effect on the skin barrier function. However, it was clear that nickel tank house workers showed higher TEWL values and lower hydration values than copper tank house workers, albeit copper tank house workers are exposed to higher sulphuric acid concentrations than nickel tank house workers, which in turn supports the conclusion mentioned above. The deteriorated skin barrier function seen in nickel tank house workers can therefore be attributed to the presence of nickel on the workers' skin, a well-known skin sensitiser.

Opsomming

Titel: Die invloed van beroepsblootstelling aan swaelsuurmis op die velafskermingsfunksie in ’n basismetaal raffinadery.

Motivering: Die vel is die primêre skeiding tussen die interne en eksterne omgewing. Skade aan hierdie grens sal lei tot nadelige gevolge vir die gesondheid, soos waterverlies deur die vel sowel as die opname van eksogene en potensieël gevaarlike stowwe. Die monitering van werknemers se vel toestand word nog nie gesien as ’n haalbare Beroepshigiëne moniterings metode nie. Hierdie studie behoort lig op die belangrikheid daarvan te werp.

Doel: Om die omvang van die moontlike negatiewe invloed van swaelsuurmis op die veltoestand en velafskermingsfunksie van die werknemers, wat by 'n basismetaal raffinadery werk, deur die konsentrasie van swaelsuurmis in die lug te korreleer met drie vel veranderlikes. Hierdie drie veranderlikes is transepidermale water verlies (TEWV), hidrasie van die stratum corneum en vel oppervlak pH. Gevolglik sal die verwantskap tussen pH en TEWV, pH en hidrasie asook TEWV en hidrasie ondersoek word.

Metodologie: Die konsentrasie van swaelsuurmis in die lug van die koper-en nikkeltenkhuise is gemeet deur die NIOSH metode 7903 vir anorganiese sure te gebruik. Metings van die velafskermingsfunksie is ook geneem om die toestand van die vel te bepaal op daardie tydstip. Drie veranderlikes is gemeet, naamlik TEWV, stratum korneum hidrasie en vel oppervlak pH. Die swaelsuurmis konsentrasies is dan gekorreleer met die vel waardes om die invloed van swaelsuurmis op die velafskermingsfunksie vas te stel. Kwalitatiewe depper monsters is geneem om te toets vir die teenwoordigheid van koper of nikkel op die vel. Dit is gedoen om twee redes: Eerstens, indien koper of nikkel teenwoordig was op die vel, kon hierdie metale opgeneem word deur die vel, wat kon bydra tot vel beskadiging. Tweedens, as die vel veranderlikes toon dat daar wel velskade plaasgevind het, kan daar ‘n groter moontlikheid wees dat hierdie metale deur die vel geabsorbeer kan word wat nadelige gevolge vir die gesondheid kan inhou.

Resultate en gevolgtrekkings: Die resultate van hierdie studie het aangedui dat die handpalm en agterkant van die hand gebiede hoë TEWL waardes en lae hidrasie

waardes toon. Dit is te verwagte siende dat hierdie gebiede blootgestel word aan meganiese wrywing deur die handskoene wat lei tot slytasie van die vel oppervlak. Geen beduidende korrelasie is gevind tussen swaelsuurmis konsentrasies in die lug en die drie gemete vel veranderlikes nie. Dit wil dus voorkom of die lae swaelsuurmis konsentrasies nie ’n beduidende invloed gehad het op die velafskermingsfunksie nie. Wat egter wel duidelik is, is dat nikkeltenkhuis werkers hoër TEWL waardes en laer hidrasie waardes het as kopertenkhuis werkers. Kopertenkhuis werkers word blootgestel aan hoër swaelsuur konsentrasies as nikkeltenkhuiswerkers wat die bogenoemde gevolgtrekking ondersteun. Die verswakte velafskermingsfunksie wat gevind is by die nikkeltenkhuis werkers kan dus toegeskryf word aan die teenwoordigheid van nikkel, ’n bekende vel sensitiseerder, op die werkers se vel.

Chapter 1

General Introduction

1.1 Introduction

South Africa is known worldwide for its abundance in natural- and mineral resources. In terms of contribution to the Gross Domestic Product (GDP), South Africa has the fifth largest mining sector in the world. According to the US Geological Survey it has the world's largest deposits of manganese and platinum group metals (PGM's), namely platinum, palladium, rhodium, ruthenium, osmium and iridium (Wilburn, 2012; South Africa.info, 2013). More than 80% of the world's platinum is found in the Bushveld Igneous Complex (BIC) in North Eastern South Africa (Nell, 2004; South Africa PGM Production, 2008).

The mining industry is a significant contributor to the country's economic activity, job creation and foreign exchange earnings, and therefore plays a major role in South Africa's socio-economic development. The mining sector has created one million jobs in South Africa, accounts for 18% of the GDP and 12% of international investments. By the end of 2011, the mining industry in South Africa was the largest contributor of broad based black economic empowerment (BBBEE), with the target for black mine ownership set at 26% by the end of 2014 (South Africa.info, 2012).

PGM containing ore is mined from opencast- and conventional mines from the UG2 and Merensky reefs, located in the BIC. This ore is then concentrated to further prepare it for the smelting process. From these concentrators the concentrate is transferred to one of three smelters, where it is flash dried, pneumatically transferred and subsequently smelted to produce an iron-nickel-copper-cobalt matte (Nell, 2004). This matte is then transferred to the Converting Process plant, where it is smelted again to remove the iron content. The remaining matte is known as converter matte (Hundermark *et al.,* 2011), and is transported to the base metal refinery where the remaining base metals are extracted and refined.

At the base metal refinery, the copper, nickel and cobalt compounds are removed from the matte, before the remaining matte (which contains concentrated PGM's) is sent to the precious metal refinery.

In both the nickel- and the copper refining tank houses, sulphuric acid is used in the electrolysis baths to produce copper- and nickel plates as the final product. Sulphuric acid mists emanate from these baths, resulting in worker exposure. Sulphuric acid can react with organic compounds which can lead to the formation of carcinogenic compounds (Luttrell, 2003). Long term exposure to strong inorganic acid mists has been known to lead to the development of laryngeal, nasal and lung cancer (Blair and Kazeroni, 1997). In 1997 the International Agency for the Research on Cancer (IARC) upgraded sulphuric acid to a Class A1 Confirmed human carcinogen (IARC, 2012).

Sulphuric acid has a very low pH, and as such is a strong corrosive agent. Skin corrosion is defined as the production of irreversible tissue damage (Kandàrova *et al.,* 2006). The effect of sulphuric acid on the skin is well known. In this study it is the effect of sulphuric acid *mist* that will be examined.

The skin is the primary barrier between a human being and the outside world. It protects the human body against physical (e.g. mechanical, thermal, and radiation), chemical (solvents and other chemical substances) and environmental elements that threaten normal health. Wherever the skin is intact, it acts as a barrier to prevent the loss of water, proteins and other components from the body (Darlenski *et al.,* 2009), as well as the entry of exogenous, and possibly toxic, substances (Proksch *et al.,* 2008) as well as the invasion by micro-organisms (Flour, 2009).

To determine the effectiveness of the skin as a barrier, certain factors such as transepidermal water loss (TEWL), stratum corneum hydration and skin surface pH can be quantified (Darlenski *et al.,* 2009).

TEWL

TEWL is the physiological loss of water vapour from the skin that is not sweat. A disruption of the barrier function of the skin will lead to an increase in TEWL (Kezic and Nielsen, 2009), whereas a lower TEWL value is characteristic of an intact skin barrier (Darlenski *et al.,* 2009). Therefore, if the skin's barrier function is compromised by chemical or physical damage, a high TEWL value is expected.

Hydration

The small amount of water that is normally lost through the skin only serves to hydrate the stratum corneum, which also allows enzymatic reactions to occur that lead to stratum corneum maturation.

Studies have shown a clear correlation between stratum corneum hydration and TEWL. A lower TEWL and normal hydration values are associated with normal healthy skin, whereas high TEWL and low hydration values are normally linked to damaged or diseased skin (Darlenski *et al.,* 2009).

Skin surface pH

Literature on the skin's natural surface pH shows no definitive value, as there are reports of the pH ranging from four to seven (Lambers *et al.,* 2006). It was found that skin with a pH lower than five is healthier than skin with a pH higher than 5 (Wagner *et al.,* 2003; Lambers *et al.,* 2006), which would mean a more intact skin barrier. Studies have also shown that a continuous elevated skin surface pH leads to a decrease in the skin barrier function and an increase in TEWL (Plasencia *et al.,* 2007).

The above mentioned three variables will be used to quantify the effect that sulphuric acid mist exposure may have on the skin barrier function of workers.

1.2 General aim and objectives

The effect of sulphuric acid on the skin is well known, therefore the general aim of this study is to determine the effect of airborne sulphuric acid *mist* on the skin health and skin barrier function.

Specific objectives:

To determine the influence of airborne sulphuric acid mist on the skin barrier function, and the effect this will have on variables such as skin hydration, transepidermal water loss and skin surface pH values over an eight hour work shift. Values of the skin variables will be correlated with the sulphuric acid mist concentrations present in the working environment to determine the effect of sulphuric acid mist on the skin condition. To determine the presence of nickel- or copper compounds on the skin by means of qualitative skin swab sampling, which could have a detrimental effect on skin health. To determine the effectiveness of control measures currently implemented in the nickel- and copper tank houses.

1.3 Hypothesis

Exposure to sulphuric acid mist will decrease skin surface pH to such a level that TEWL will increase and the level of skin hydration will decrease, indicating a decrease in the skin barrier function during a work day.

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Chapter 2

Literature overview

2.1. Literature overview

2.1.1. Introduction

This literature overview will provide a basic understanding of the platinum mining industry of South Africa, as well as the properties of sulphuric acid, copper and nickel and their effects on the human body. Transepidermal water loss (TEWL), skin hydration and skin surface pH will also be discussed in detail.

2.1.2. Mining industry in South Africa

The precious metal platinum is found naturally along with five other metals, namely palladium, rhodium, ruthenium, osmium and iridium. Together these metals are known as platinum group metals (PGM). PGM's are mined at open cast mines – such as Pilanesberg platinum mine and Unki in Zimbabwe – as well as in underground mines, the deepest of which is 2.2 km deep (Creamer, 2007; South African PGM Production, 2008; Louw, 2013). More than 80% of the world's platinum is found in the Bushveld Igneous Complex (BIC) (Nell, 2004). Platinum has unique qualities, such as a high melting temperature and corrosion- and oxidation resistance, and because of these novel qualities it is used in many industries, including the health industry (pacemaker batteries, cancer medication such as Oxiplatin, crowns and other dental applications), the electronics industry (computer hard drives, fuel-cells) and the automotive industry (three-way catalysts, which reduce the amount of carbon monoxide and other gasses in engine emissions), as well as many other uses (Creamer, 2006).

2.1.3. Platinum mining process overview

Platinum mining process

Ore that is mined from the Merensky and UG2 reefs is concentrated in preparation for the smelting process, which further concentrates the PGM's to prepare them for the refining process. The ore from these two reefs is mixed to balance the amount of chromium oxide (Cr_2O_3) and silica present in the concentrate. This is done because the ore from the UG2 reef contains more Cr_2O_3 than the Merensky ore, and ore containing a concentration of Cr_2O_3 that is too high will melt at temperatures higher than is optimal for the furnaces. Too much Cr_2O_3 will furthermore saturate the slag and form a spinel, which will lead to an unclean matte-slag separation i.e. the matte will be contaminated with Cr_2O_3. Higher silica concentrations will lead to a more viscous slag. The concentrate is transported to one of three smelters where it is flash dried at a temperature of between 900 – 1100 °C to remove all moisture. After drying of the concentrate, it is pneumatically transferred to an electric, six-submerged-electrode arc furnace where it is smelted at temperatures of up to 1600 ºC to produce an iron-nickel-copper-cobalt matte (Nell, 2004). This matte is then tapped and either granulated or cast and crushed after which the matte is transported to the converting process plant, where it is smelted again to remove all iron compounds to further concentrate the PGM's (Hundermark *et al.,* 2011). This matte is then known as converter matte, which will be bottom cast and slow-cooled before being transported to the base metal refinery for the next step in PGM isolation and refining as can be seen in Figure 1.

At the base metal refinery, all copper, nickel and cobalt compounds are removed from the matte before sending the remaining matte to the precious metal refinery for the final phase of refining the six precious metals. At the nickel tank house, the feed is prepared by filtration of the matte through Funda disc filters (Pavlides, 2008). This filtered feed is then pH adjusted by adding spent and/or new sulphuric acid to obtain a pH of 3.2. The feed temperature is then raised to 50 – 55 °C where it passes into a header tank and is then distributed to all the cells. The feed flow per cathode is ± 15 L per hour with 48 cathodes per cell. Nickel ions in the feed are attracted to the cathode while O_2 and H^+ gas is produced at the anode. Spent sulphuric acid overflows and is subsequently pumped away. The nickel sheet is removed from the cathode as the final product by the workers after which the cathode plate is re-used (Varty, 2013). At the copper tank house, the feed is prepared by filtration through Shibler filters, and this feed is not pH adjusted. The feed temperature is then also raised to 50 – 55 °C. From here it passes into the copper feed tank from where it is distributed through a carousel system to the cells. The flow rate per cell is ± 333 L per hour with 103 cells in total. Copper ions are attracted to the cathode while O_2 and H^+ gas is produced at the anode. The spent sulphuric acid overflows and is pumped to the Leach section. The copper sheet is removed from the cathode as the final product by the workers while the cathode is re-used (Van der Linde, 2013).

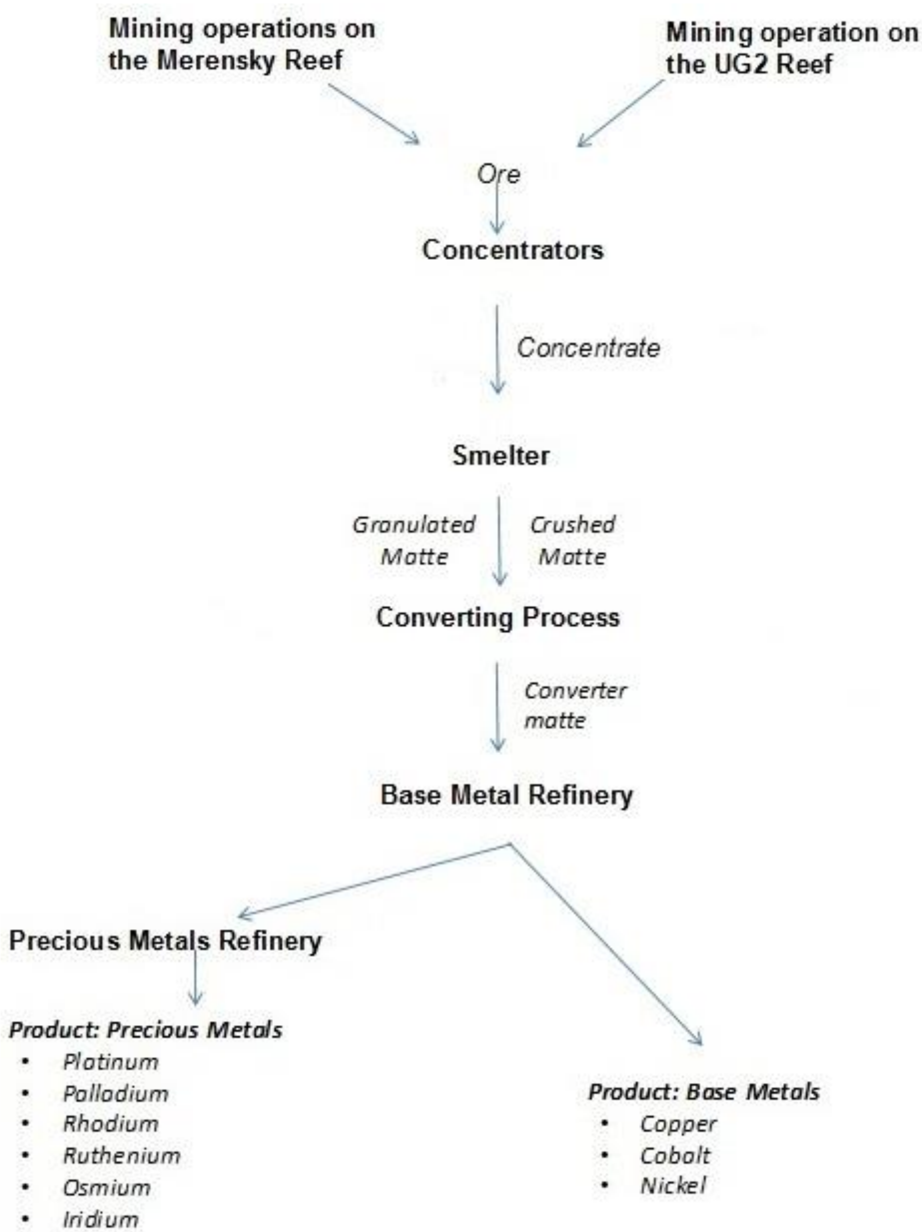

Figure 1: The platinum mining process flow.

2.1.4. Skin exposure in the mining industry

Both tank houses have effective inhalation exposure protection in place in the form of ventilation hoods located inside the cells (Varty, 2013) to extract the sulphuric acid mist before reaching the workers, as well as personal respiratory protection, which is readily available to the workers. Workers still experience skin exposure whenever the cells are inspected and possible faults are repaired, as well as during cell harvesting, which is a labour intensive process (Pavlides, 2008).

Sulphuric acid causes skin erosion (Kandàrova *et al*., 2006), yet it does not have a skin notation in South African legislation. This is because a skin notation only implies that the compound may be absorbed systematically and have a detrimental effect on the person's health as a whole, as is the case with volatile organic compounds, and not a detrimental effect on the skin alone (Klonne, 2003, Schaper and Bisesi, 2003). To maximise the protection of worker health, the skin notation definition needs to be altered to include the effect of skin erosion, irritation and sensitisation as well. Skin erosion will increase the permeability of the skin to exogenous substances which could have a detrimental systemic effect.

Automation of this process would greatly reduce personal exposure, but seeing as labour costs in South Africa is low compared to more developed countries, it would therefore not be economically viable to install these machines (Pavlides, 2008).

2.1.5. Skin Physiology

Sulphuric acid (H_2SO_4) is produced in large quantities around the world and is used in a wide variety of industries (Gangopadhyay and Das, 2008). Sulphuric acid mist has a very low pH and is a strong corrosive agent. Skin corrosion is defined as the production of irreversible tissue damage (Kandàrova *et al*., 2006). If the sweat on the skin surface has an extremely low (pH $\leq$ 2.0) or high (pH $\geq$ 11.5) pH, irreversible damage will be done to the keratin in the skin, leading to a more permeable skin barrier (Grasso and Lansdown, 1972; Schuhmacher-Wolz *et al.,* 2003; Li *et al.,* 2012). Over-exposure to sulphuric acid mist and -vapour can cause chemical burns to the lungs and bronchial passageways, skin and the eyes (Benomran *et al.*, 2008). Concentrated H_2SO_4 will react violently with water molecules trapped in the stratum corneum and skin damage therefore occurs via two mechanisms: chemical burns and the release of heat through the reaction of acid with water (Gangopadhyay and Das, 2008).

The skin is the primary barrier between a human being and the outside world. It protects the human body against physical (e.g. mechanical, thermal, and radiation), chemical (solvents and other chemical substances) and environmental elements that threaten normal health. Wherever the skin is intact, it acts as a barrier to prevent loss of water, proteins and other components of the organism (such as serum proteins) (Darlenski *et al.,* 2009), as well as prevent the entry of exogenous, and possibly toxic, substances (Proksch *et al*., 2008) and invasion by micro-organisms (Flour, 2009).

The skin is an organ with both protective and defensive functions. The stratum corneum is only 15 µm thick and comprises of pentagonal and/or hexagonal arranged corneocytes in a lipid matrix (Hadgraft and Lane, 2009). These corneocytes are formed by keratinocytes that differentiate into corneocytes that have no nucleus. The corneocytes also have a layer of hydrophobic lipids surrounding them, thereby further inhibiting water loss. Keratin filaments in the corneocytes react with the matrix protein known as filaggrin to form tight bundles. This causes the cell to form a long, flat shape (Proksch *et al.,* 2008), leading to the popular description of a “brick-and-mortar” appearance (Hadgraft and Lane, 2009). The corneodesmosomes also assist in keeping the cells of the stratum corneum tightly packed. The top layer of corneocytes is constantly being replaced by younger cells from deeper lying cellular layers of the epidermis by a process known as desquamation. Desquamation requires that the corneodesmosomes be broken down by serine proteases, a process controlled by the availability of free water in the inter-cellular spaces (Harding *et al.,* 2000). A high instance of transepidermal water loss (TEWL) will then logically lead to a lower rate of desquamation, leading to the appearance of dry and/or flaky skin (Verdier-Sévrain and Bonté, 2007). Damage to the skin, however small, can lead to a large increase in trans-dermal absorption of exogenous substances (Filon *et al.,* 2009).

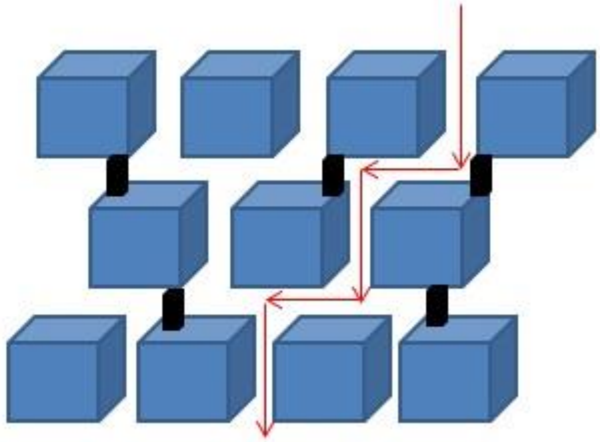

Figure 2: Brick-and-mortar composition of the stratum corneum. Blue rectangles represent the flattened corneocytes and black rectangles represent the corneodesmosomes. The red arrow represents the main pathway of exogenous substance absorption i.e. not through the corneocytes, but rather through the spaces between them. (Hadgraft and Lane, 2009).

The stratum corneum plays a major role in the degree of skin permeability, and this permeability can be altered by changes in climate, physical stressors and a variety of skin- and systemic diseases (Darlenski *et al.*, 2009). Permeability is determined by the number of corneocyte layers and the size of the corneocyte (the larger the corneocyte, the longer the path of diffusion). The size of the corneocytes is determined by the area of the body in which they are found (e.g. corneocytes in the skin of the face are smaller than the corneocytes in the skin of the hand) (Hadgraft and Lane, 2009), as well as how densely packed they are.

This study was done in a South African base metal refinery; the difference between stratum corneum properties seen in different ethnicities has to be taken into account. Previous studies have found that in both cases of chemical and mechanical damage, people with darker skin show a better stratum corneum functioning than light skinned people (Rawlings, 2006), leading to a lower level of TEWL than observed in Caucasians, Asians and Hispanics (Singh *et al.,* 2000). In this study, only African men were sampled as they are the only race- and gender group involved with the manual handling of the copper- and nickel sheets in the tank houses.

To determine the effectiveness of the skin as a barrier, certain factors such as TEWL, stratum corneum hydration and skin surface pH can be quantified (Darlenski *et al.*, 2009), as well as stratum corneum thickness seeing as there is a negative correlation between TEWL values and corneocyte size (Machado *et al.,* 2010). Determining stratum corneum thickness however requires invasive methods, which are unpleasant for test subjects, and as such are avoided by researchers. Skin diseases, such as atopic eczema and contact dermatitis, will lead to a change in the epidermal barrier function of the skin. These diseases will inevitably lead to an increase in water loss through the stratum corneum (Cork, 1997).

Factors that determine the rate of absorption of substances through the skin – and as such the degree with which the skin's barrier function has been compromised – can be divided into two main groups: exogenous and endogenous factors. Exogenous factors include the dose, the substances' molecular volume, the effect of counter-ions, the polarity, the ion's valence, reactivity with proteins, solubility and pH dependence (Li *et al.,* 2012). The endogenous factors include the skin's age (as explained under *Hydration* later), the anatomical site, the degree of homeostatic control, the number of skin layers and the rate of oxidation and reduction in the skin. Quantifying percutaneous absorption is always difficult, as the above mentioned factors show a very high degree of variability, even more *in vivo* than *in vitro* (Hostynek, 2003).

Of the above mentioned factors, the most prevalent ones that will play a role in percutaneous absorption in this study will include the dose, the time of exposure (McDougal and Boeniger, 2002) and the pH dependence. Filon *et al.* (2009) stated that the pH of the solution that the compound is in, in this case sweat, determines the state of ionisation, which will influence the rate of percutaneous absorption. The presence of counter ion competition should also be kept in mind, but is not of concern in this specific study; salts that have small differences in chemical composition e.g. polarity, could have very large absorption rate differences. For example, nickel sulphide ($NiSO_4$) (formed by Ni^{2+} + H_2SO_4) and nickel chloride ($NiCl_2$) (formed by Ni^{2+} + NaCl in sweat), as is the case with copper ions. A study by Tanojo *et al.* (2001) showed that $NiSO_4$ had a higher permeability constant through human skin than $NiCl_2$. A study by Hostynek and Maibach (2006) showed that copper sulphate ($CuSO_4$) had a higher permeability constant than copper chloride ($CuCl_2$) when both substances were applied to the skin in a petroleum gel.

2.1.6 Skin parameters

TEWL, skin pH and skin hydration are three important factors that can be used to determine the condition of the human skin, and therefore the condition and effectiveness of the skin's barrier.

2.1.6.1 TEWL

TEWL is the physiological loss of water vapour from the skin in the absence of sweat gland activity. A disruption of the barrier function of the skin will lead to an increase in TEWL (Kezic and Nielsen, 2009), whereas a lower TEWL value is characteristic of an intact skin barrier (Darlenski *et al.*, 2009). If the skin's barrier function is compromised by chemical or physical damage, a high TEWL value is therefore expected. No accurate index could be found for the Vapometer specifically, although values of up to 13 – 15 $g/m^2/h$ are accepted as normal for Africans according to Singh *et al.* (2000); therefore values of > 15 indicate elevated water loss through the stratum corneum.

TEWL is directly proportional to air movement across the skin and indirectly proportional to environmental temperature and humidity (Machado *et al.*, 2010). Normal skin allows water loss only in small amounts as it is needed to ensure maturation of the stratum corneum whereas in dry, flaky and damaged skin the water loss is much higher (Mündlein *et al.,* 2008; Rawlings *et al*., 2008). TEWL measurements allow for the discovery of disturbances in the protective barrier function of skin at an early stage, even before they are visible (Mündlein *et al.,* 2008).

It can also be used to indirectly predict the influence of substances that the skin is exposed to, such as (in the case of this study) copper and nickel- ions and salts as well as H_2SO_4 (Darlenski *et al*., 2009).

The determination of TEWL is therefore an important parameter used to investigate skin irritation and changes in skin barrier permeability (Mündlein *et al*., 2008; Darlenski *et al*., 2009) that occur as a result of various physical and chemical disturbances. As an example of this, Eberlein-König *et al.* (2000) found an increased TEWL value in adult patients with eczematous skin lesions and dry skin.

Evapirometry is the accepted method of monitoring changes in TEWL to determine the extent of the skin's functioning as a barrier (Rawlings *et al.,* 2008).

2.1.6.2 Skin Hydration

The small amount of water that is normally lost through the skin only serves to hydrate the stratum corneum, which also allows enzymatic reactions to occur that lead to stratum corneum maturation. The degree of water retention depends on how tightly packed the corneocytes of the stratum corneum are. It should be noted that three other factors also play a role in the level of skin hydration: Firstly, intercellular lamellar (adjacent to one another) lipids, organised in an orthorhombic gel phase. Second, the longer the diffusion path length through skin, the slower the rate of water loss will be, and finally the natural moisturising factor (NMF) (Rawlings and Harding, 2004). The NMF is a mixture of low-molecular weight, water soluble molecules formed by corneocytes by the catabolism of the histidine-rich protein filaggrin, which will allow the skin to remain hydrated even at low relative humidity (Scott and Harding, 1986*)*. There is a decrease in the amount of NMF with increasing age, due to the decrease in profilaggrin production (Rawlings and Harding, 2004). This leads to a decrease in skin barrier function with increasing age.

There generally exists a correlation between stratum corneum hydration and TEWL. Lower TEWL and normal hydration values are associated with normal healthy skin, whereas high TEWL and low hydration values are normally linked to damaged or diseased skin. The physical appearance of skin is also important as there is a greater chance that larger volumes of water will be lost through dry and flaky skin (Darlenski *et al.*, 2009).

2.1.6.3 Skin surface pH

As sulphuric acid mist has a very low pH and can have a large influence on skin surface pH, it will be discussed more in depth. Literature on the skin's natural surface pH shows a large variation in skin surface pH from four to seven depending on age, gender and body area (Lambers *et al.,* 2006). Lambers *et al.* (2006) and Filon *et al.* (2009) however determined that the average skin surface pH is 4.7, or below five for that matter. It was found that skin with a pH lower than five is seen as an intact skin with a lower TEWL rate than skin with a surface pH higher than five (Wagner *et al.,* 2003; Lambers *et al*., 2006). This low pH is ideal for the enzymes that process the lipids that ultimately form the skin barrier, and a neutral pH will inhibit the function of these repairing enzymes (Mauro *et al.,* 1998; Flour, 2009). The acidic pH also stimulates the catabolic enzymes that convert filaggrin into NMF, as was explained earlier (Lambers *et al.,* 2006). Lambers *et al.* (2006) also showed that skin with a surface pH of lower than five showed higher levels of hydration, as well as increased resistance to the SLS (sodium lauryl sulphate) – induced irritant dermatitis test.

The effect of a lower skin pH that is optimal for skin barrier functioning can be seen in new-born babies; neonates have an elevated skin surface pH, and as such, are more susceptible to irritant dermatitis (Plasencia *et al.,* 2007). Plasencia *et al.* (2007) also showed that continuous skin surface pH elevation from five to eight leads to a decrease in the skin barrier function and an increase in TEWL. This trend is consistent with other literature, stating that a decrease in barrier properties of the skin can be observed with a more alkaline surface pH (Gammelgaard *et al*., 1992; Hostynek, 2003). This study should shed some light on the true effect of sulphuric acid mist on the skin, in concentrations as seen in these refineries: either the acid lowers the skin surface pH to such a level that the skin barrier function may be improved, or to such a low pH that skin erosion may occur.

The effect of sweat on the skin's surface pH also has to be taken into account, seeing as this pH is usually seen in the ranges of 4 – 5.5, but these levels can drop even lower during heightened physical activity. More acidic sweat will oxidise metal ions into their ionised state (Filon *et al.,* 2009) which will increase skin absorption due to the increased solubility (Hadgraft and Valenta*,* 2000) even though the increased solubility leads to a decrease in permeability (Li *et al.,* 2012). Therefore while the acid mists may improve skin barrier function, they will also increase the rate of metallic ion absorption through the skin. The skin irritation potential of compounds containing copper is as yet still undetermined (Hostynek and Maibach, 2004), but nickel is a well-known skin sensitiser (Du Plessis *et al.*, 2010).

Failure of the stratum corneum to retain water (lower hydration) causes dryness and impairs the function of the skin barrier (Kezic and Nielsen, 2009), but percutaneous absorption will also be affected by the physicochemical properties (hydrophilicity or lipophilicity) of these compounds. The stratum corneum is lipophilic, and as such lipophilic compounds will easily move through the skin barrier. Most compounds tend to have both lipophilic and hydrophilic characteristics, but compounds that are too hydrophilic will not penetrate the stratum corneum, and compounds that are too lipophilic will penetrate the stratum corneum and never escape it (Naik *et al.,* 2000). Nielsen and Nielsen (2007) also proved this by showing that compounds with high log P_{ow} values, that is to say more lipophilic, tend to penetrate all the way into the deeper dermis, whereas compounds with low log P_{ow} values are more hydrophilic and only penetrate into the epidermis. In other words, compounds that are in the extremes of hydro- or lipophilicity never truly penetrate the skin (Nielsen and Nielsen, 2007), and as they are not absorbed into the blood stream, they cannot exert toxic effects. Nielsen and Nielsen (2007) showed that hydrophilic compounds do not penetrate the skin as easily as lipophilic compounds, but mechanical and chemical damage to the skin will increase the penetration rates of hydrophilic compounds exponentially. In the case of lipophilic compounds, skin damage only increased penetration two-fold.

As mentioned before, quantifying *in vivo* percutaneous absorption is a challenge as the factors that determine the rate of penetration show a high degree of variability. For example, Hawkins and Reifenrath (1984) showed that the skin penetration rate for the lipophilic compound N,N-diethyl-m-toluamide more than doubled when the air temperature was increased from 20°C to 32°C. Increases in air humidity lead to an increase of skin penetration by hydrophilic compounds, but had no or little effect on lipophilic compounds (Hawkins and Reifenrath, 1984).

Cutaneous blood flow is relatively efficient in removing xeno-compounds from the skin (McCarley and Bunge, 2001). The resulting diffusion gradient would increase percutaneous absorption of compounds, both hydrophilic and lipophilic. If the blood flow is therefore high enough, the concentration of these compounds in the skin would be lowered to such an extent that there would be zero resistance to percutaneous absorption – other than the resistance already offered by the stratum corneum itself (Wiechers, 1989). A reduction in the barrier function of the skin will also be indicated by an increase in the TEWL value. If the skin's barrier function is compromised by chemical or physical damage, a high TEWL and a low hydration value is expected. Once the barrier is less effective it becomes more permeable to substances - for instance copper and nickel - leading to a higher risk for systemic toxicity (Kezic and Nielsen, 2009).

2.1.7 Copper

Copper is absorbed into the circulation from the gastro-intestinal system, the lungs or through the skin (Hostynek and Maibach, 2006). Copper sulphate leads to the formation of free radicals (Macomber *et al.,* 2007) as well as changes in nucleic acid structure, causing DNA damage, when high concentrations are present in the cell (SalehaBanu *et al.*, 2004). It was proven that copper miners have an increased risk to develop lung cancer due to inhalation of copper ore dust (Chen *et al.,* 1993).

Letelier *et al.* (2005) however showed that copper also causes cell damage by binding to cellular proteins at random. Immediately after the ingestion of copper, various symptoms such as a metallic taste, abdominal pain, diarrhoea and/or vomiting may appear (SalehaBanu *et al.*, 2004). According to a study done by Kumar and Rana *et al.* (1982), rats treated with copper sulphate by means of force-feeding showed a decrease in skeletal growth and weight gain, as well as excessive copper accumulation in the liver and kidneys. Another study done by SalehaBanu *et al.* (2004) showed excessive DNA damage in the leukocytes of mice treated orally with high concentrations of $CuSO_4$ ranging from 1.25 to 12.5 mg/kg body weight. The degree of DNA damage showed a clear dose-response correlation i.e. as the dose increased, so did the DNA damage (p <

0.05). High copper levels led to the formation of reactive oxygen species (via the Fenton reaction) which can lead to DNA damage. High levels may also cause changes in nucleic acid structure, leading to a change in gene expression (SalehaBanu *et al.*, 2004). Copper, and its salts, are therefore viewed as genotoxic at high concentrations and exposure should be brought to a minimum. Ironically, copper is a catalytic cofactor in the superoxide dismutase anti-oxidant enzyme, which breaks down reactive oxygen species (Pan and Loo, 2000). It should be noted that several other studies have been conducted on the genotoxicity of $CuSO_4$ and that results are inconsistent (SalehaBanu *et al.*, 2004).

2.1.8 Nickel

Larese *et al.* (2007) proved that nickel dust will be oxidised in sweat into the Ni^{2+} ion that can easily permeate the skin, and a study by Tanojo *et al.* (2001) proved that nickel salts in a watery solution (such as sweat) also permeate the stratum corneum quite easily.

Nickel will lead to the development of allergic contact dermatitis in up to 10% of the general population, and up to 15% of women (Filon *et al.,* 2009), with 30 – 40% of people developing hand eczema due to nickel exposure (Larese *et al*., 2007). A study by Ikarashi *et al.* (1996) also showed dermal exposure to $NiSO_4$ to have a sensitising effect.

2.1.9 Sulphuric acid

Dermal exposure to sulphuric acid may damage the skin leading to a decrease in the skin's barrier function and consequently an increase in TEWL. No occupational exposure limits or skin notations exist for dermal exposure, and as such the specific risks of dermal exposure to sulphuric acid cannot be precisely quantified (McDougal and Boeniger, 2002).

Occupational hygiene has predominantly focused on inhalation exposures because this was seen as the most important route of exposure, thereby disregarding dermal and ingestion exposure (Du Plessis *et al.*, 2010). Regardless, it is necessary to place emphasis on investigating factors that determine the integrity and health of the skin (Poet and McDougal, 2002), especially in the chemical industry where workers are exposed to a variety of chemicals every day. It is necessary to evaluate their skin condition regularly.

Sulphuric acid has a TWA-OEL of 1 mg/m^3 and no specified Short Term OEL value (Regulations for Hazardous Chemical Substances, 1995), mirroring recommended exposure level of the NIOSH (NIOSH, 2003). The ACGIH however changed the Threshold Limit Value (TLV) of sulphuric acid from 1 mg/m^3 to 0.2 mg/m^3 in 2005 (ACGIH, 2005). Luttrell (2003) does however stipulate a short term OEL value of 3 mg/m^3. Several studies have also found that sulphuric acid is a class A2 (suspected) carcinogen, but the IARC stated in their 1997 report that strong inorganic acid mists such as sulphuric acid mists fall under group 1, which are defined as human carcinogens (IARC, 1997). This was reconfirmed in their 2012 monograph on carcinogens in the workplace (IARC, 2012). Sulphuric acid reacts with organic compounds to form carcinogenic and mutagenic compounds (Luttrell*,* 2003); long term exposure to sulphuric acid has been associated with laryngeal cancer (Blair and Kazeroni, 1997) and other areas of the respiratory tract (IARC, 2012). Other studies, however, show that sulphuric acid's carcinogenicity can however be attributed to its low pH, rather than the above mentioned chemical reactions (OECD, 2001).

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Chapter 3

Article

The influence of occupational exposure to sulphuric acid mist on skin barrier function in a base metal refinery

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Although the instructions for authors state that illustrations, tables and graphs are to be submitted as separate pages, for the purpose of this study the tables and figures will be inserted within the results section of Chapter 3 in order to improve readability. It is acknowledged that the article exceeds the limit for the number of words used due to the comprehensive nature of the study. The article will be shortened before submission.

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The influence of occupational exposure to sulphuric acid mist on skin barrier function in a base metal refinery

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Abstract

Introduction: This study was performed to investigate the effect, if any, that sulphuric acid mist has on the skin barrier function of workers exposed in an occupational setting. Workers of a South African base metals refinery are exposed to sulphuric acid mist during the electrowinning process of copper and nickel plates. The objective of this study was to assess the effect of the sulphuric acid mists on the skin barrier function of these refinery workers.

Methodology: Eleven workers from the copper tank house and eight workers from the nickel tank house volunteered to participate in this study. Personal sulphuric acid mist samples were taken on these workers, as well as the measurement of three skin variables used to assess skin health, namely TEWL, skin hydration and skin surface pH. The skin measurements were taken before the shift started, at the start of the tea break and at the end of the shift. The body areas where measurements were performed were divided into two groups, namely the exposed areas (forehead, cheek, neck) and the covered areas (palm, back of hand, inner forearm). Two sulphuric acid samples were taken per worker per shift, one from the beginning of the shift to the tea break, and the second from the end of the tea break to the end of the shift. Qualitative swab samples were also taken to determine if copper or nickel was present on the skin. This was done to determine if the presence of these metals played a role in skin barrier function deterioration, or if only sulphuric acid had this effect.

Results: Palm and back of hand showed the highest TEWL readings and the lowest hydration readings. This is to be expected as these areas are subjected to mechanical friction by the PPE leading to wear and tear on the skin surface. Nickel tank house workers showed, on average, higher TEWL readings and lower hydration readings than the copper tank house workers. Qualitative tests showed negative results for copper in the copper tank house workers throughout the shift, but results were positive for the presence of nickel on nickel tank house workers' skin. It is believed that this is due to the presence of nickel, and not because of sulphuric acid, seeing as sulphuric acid mist levels encountered in the copper tank house area (0.11 mg/m^3) are much higher than in the nickel tank house (0.031 mg/m^3). Subsequently, this effect could be seen on the exposed body areas, seeing as the skin surface pH readings on the forehead, cheek and neck areas of copper tank house workers were much lower than those of nickel tank house workers.

Conclusion: Few statistically meaningful correlations could be found between sulphuric acid mist concentration and skin barrier function. Based on Dalgard score results, it is clear that many workers in the nickel tank house are affected by the nickel found on their skin, with many complaining of itchy skin and rashes, rather than the sulphuric acid mists they were exposed to.

Key words: sulphuric acid, TEWL, skin surface pH, skin hydration, skin barrier function

3.1 Introduction

Sulphuric acid (H_2SO_4) is produced in large quantities around the world and is used in a wide variety of industries (Gangopadhyay and Das, 2008). Sulphuric acid mist has a very low pH and is a strong corrosive agent. Skin corrosion is defined as the production of irreversible tissue damage (Kandàrova *et al*., 2006). If the sweat on the skin surface has an extremely low (pH ≤ 2.0) or high (pH ≥ 11.5) pH, irreversible damage will be done to the keratin in the skin, leading to a more permeable skin barrier (Grasso and Lansdown, 1972; Schuhmacher-Wolz *et al.,* 2003; Li *et al.,* 2012). Over-exposure to sulphuric acid mist and -vapour can cause chemical burns to the lungs and bronchial passageways, skin and the eyes (Benomran *et al.*, 2008). Concentrated H_2SO_4 will react violently with water molecules trapped in the stratum corneum and skin damage therefore occurs via two mechanisms: chemical burns and the release of heat through the reaction of acid with water (Gangopadhyay and Das, 2008).

The skin is the primary barrier between a human being and the outside world. It protects the human body against physical (e.g. mechanical, thermal, and radiation), chemical (solvents and other chemical substances) and environmental elements that threaten normal health. Wherever the skin is intact, it acts as a barrier to prevent loss of water, proteins and other components of the organism (such as serum proteins) (Darlenski *et al.,* 2009), as well as prevent the entry of exogenous, and possibly toxic, substances (Proksch *et al*., 2008) and invasion by micro-organisms (Flour, 2009).

The stratum corneum plays a major role in the degree of skin permeability, and this permeability can be altered by changes in climate, physical stressors and a variety of skin- and systemic diseases. To determine the effectiveness of the skin as a barrier, certain factors such as TEWL, stratum corneum hydration and skin surface pH can be quantified (Darlenski *et al.*, 2009).

This study was done in a South African base metal refinery; the difference between stratum corneum properties seen in different ethnicities has to be taken into account. Previous studies have found that in both cases of chemical and mechanical damage, people with darker skin show a better stratum corneum functioning than light skinned people (Rawlings, 2006), leading to a lower level of TEWL than observed in Caucasians, Asians and Hispanics (Singh *et al.,* 2000).

Factors that determine the rate of absorption of substances through the skin – and as such the degree with which the skin's barrier function has been compromised – can be divided into two main groups: exogenous and endogenous factors. Exogenous factors include the dose, the substances' molecular volume, the effect of counter-ions, the polarity, the ion's valence, reactivity with proteins, solubility and pH dependence (Li *et al.,* 2012). The endogenous factors include the skin's age (as explained under *Hydration* later), the anatomical site, the degree of homeostatic control, the number of skin layers and the rate of oxidation and reduction in the skin. Quantifying percutaneous absorption is always difficult, as the above mentioned factors show a very high degree of variability, even more *in vivo* than *in vitro* (Hostynek, 2003).

Of the above mentioned factors, the most prevalent ones that will play a role in percutaneous absorption in this study will include the dose, the time of exposure (McDougal and Boeniger, 2002) and the pH dependence. Filon *et al.* (2009) stated that the pH of the solution that the compound is in, in this case sweat, determines the state of ionisation, which will influence the rate of percutaneous absorption.

TEWL, skin pH and skin hydration are three important factors that can be used to determine the condition of the human skin, and therefore the condition and effectiveness of the skin's barrier.

TEWL is the physiological loss of water vapour from the skin in the absence of sweat gland activity. A disruption of the barrier function of the skin will lead to an increase in TEWL (Kezic and Nielsen, 2009), whereas a lower TEWL value is characteristic of an intact skin barrier (Darlenski *et al.*, 2009). If the skin's barrier function is compromised by chemical or physical damage, a high TEWL value is therefore expected.

Normal skin allows water loss only in small amounts as it is needed to ensure maturation of the stratum corneum whereas in dry, flaky and damaged skin the water loss is much higher (Mündlein *et al.,* 2008; Rawlings *et al*., 2008).

Skin hydration is defined as the small amount of water that is normally lost through the skin that serves to hydrate the stratum corneum, which also allows enzymatic reactions to occur that lead to stratum corneum maturation.

There generally exists a correlation between stratum corneum hydration and TEWL. A lower TEWL and normal hydration values are associated with normal healthy skin, whereas high TEWL and low hydration values are normally linked to damaged or diseased skin. The physical appearance of skin is also important as there is a greater chance that larger volumes of water will be lost through dry and flaky skin (Darlenski *et al.*, 2009).

As sulphuric acid mists have a very low pH and can have a large influence on skin surface pH, it will be discussed more in depth. Literature on the skin's natural surface pH shows a large variation in skin surface pH from four to seven depending on age, gender and body area (Lambers *et al.,* 2006). Lambers *et al.* (2006) and Filon *et al.* (2009) however determined that the average skin surface pH is 4.7, or below five for that matter. It was found that skin with a pH lower than five is seen as an intact skin with a lower TEWL rate than skin with a surface pH higher than five (Wagner *et al.,* 2003; Lambers *et al*., 2006). This low pH is ideal for the enzymes that process the lipids that ultimately form the skin barrier, and a neutral pH will inhibit the function of these repairing enzymes (Mauro *et al.,* 1998; Flour, 2009).

This study should shed some light on the true effect of sulphuric acid mist on the skin, in concentrations as seen in these refineries: either the acid lowers the skin surface pH to such a level that the skin barrier function may be improved, or to such a low pH that skin erosion might occur.

The effect of sweat on the skin's surface pH also has to be taken into account, seeing as this pH is usually seen in the ranges of 4 – 5.5, but these levels can drop even lower during heightened physical activity. More acidic sweat will oxidise metal ions into their ionised state (Filon *et al.,* 2009) which will increase skin absorption due to the increased solubility (Hadgraft and Valenta*,* 2000) even though the increased solubility leads to a decrease in permeability (Li *et al.,* 2012). Therefore while the acid mists may improve skin barrier function, they will also increase the rate of metallic ion absorption through the skin. The skin irritation potential of compounds containing copper is as yet still undetermined (Hostynek and Maibach, 2004), but nickel is a well-known skin sensitiser (Du Plessis *et al.*, 2010).

Cutaneous blood flow is relatively efficient in removing xeno-compounds from the skin (McCarley and Bunge, 2001). The resulting diffusion gradient would increase percutaneous absorption of compounds, both hydrophilic and lipophilic. If the blood flow is therefore high enough, the concentration of these compounds in the skin would be lowered to such an extent that there would be zero resistance to percutaneous absorption – other than the resistance already offered by the stratum corneum itself (Wiechers, 1989). A reduction in the barrier function of the skin will also be indicated by an increase in the TEWL value. If the skin's barrier function is compromised by chemical or physical damage, a high TEWL and a low hydration value is expected. Once the barrier is less effective it becomes more permeable to substances - for instance copper and nickel - leading to a higher risk for systemic toxicity (Kezic and Nielsen, 2009).

Copper is absorbed into the circulation from the gastro-intestinal system, the lungs or through the skin. Copper sulphate leads to the formation of free radicals (Macomber *et al.,* 2007) as well as changes in nucleic acid structure, causing DNA damage, when high concentrations are present in the cell. It should be noted that several other studies have been conducted on the genotoxicity of copper sulphate ($CuSO_4$) and that results are inconsistent (SalehaBanu *et al.*, 2004).

Larese *et al.* (2007) proved that nickel dust will be oxidised in sweat into the Ni^{2+} ion that can easily permeate the skin, and a study by Tanojo *et al.* 2001 proved that nickel salts in a watery solution (such as sweat) also permeate the stratum corneum quite easily.

Nickel will lead to the development of allergic contact dermatitis in up to 10% of the general population, and up to 15% of women (Filon *et al.,* 2009), with 30 – 40% of people developing hand eczema due to nickel exposure (Larese *et al*., 2007). A study by Ikarashi *et al.* (1996) also showed dermal exposure to $NiSO_4$ to have a sensitising effect.

The effect of sulphuric acid on the skin is well known, therefore the general aim of this study is to determine the effect of airborne sulphuric acid *mist* on the skin health and skin barrier function.

Specific objectives of this study are to; firstly, determine the influence of airborne sulphuric acid mist on the skin barrier function, and the effect this will have on variables such as skin hydration, transepidermal water loss and skin surface pH values over an eight hour work shift. Secondly, to correlate values of the skin variables with the sulphuric acid mist concentrations present in the working environment to determine the effect of sulphuric acid mist on the skin condition. Thirdly, to determine the presence of nickel- or copper compounds on the skin by means of qualitative skin swab sampling, which could have a detrimental effect on skin health. Fourthly, to determine the effectiveness of control measures currently implemented in the nickel- and copper tank houses.

3.2 Methodology

Purpose

During this study the skin variables mentioned in the literature were quantified and the concentration of sulphuric acid mist in the air of the work environment at a nickel and copper base metal refinery was determined.

Personal respiratory monitoring was done in the nickel and the copper tank houses because the two tank houses have different exposure control mechanisms for sulphuric acid mists; polypropylene beads in the copper tank house and anode bags in the nickel tank house. The airborne sampling results were used to determine which of the two proved to be more effective.

Study population

In the copper tank house there were sixteen workers per shift, and by using technical appendix A in NIOSH's Occupational Exposure Sampling Strategy Manual (OESSM) to get the 90th percentile values, eleven workers were monitored. The nickel tank house is more modern and as such the processes are automated, requiring a smaller workforce to be present. In this case an availability study was performed; meaning all eight of the workers were monitored. Test subjects in this study were all tank house operators, that is to say the workers performing the manual labour on the cells (loading, inspections and harvesting). Process supervisors were not included in the Similar Exposure Groups (SEG) as they do not take part in the above mentioned aspects of manual labour in the tank houses. The ages of the subjects working in the copper and nickel tank houses were 42 ± 10.73 and 30.13 ± 4.67years of age with work experience of 15.62 ± 11.48 and 4.25 ± 3.37 years respectively. The difference is due to the fact that the nickel tank house is a new structure and therefore employs younger employees.

Workers at both tank houses are equipped with the same personal protective equipment (PPE) consisting of a two piece acid resistant overall, acid resistant safety boots and disposable FFP-2 half face masks. Two types of gloves are available, namely latex gloves for when performing routine work in the tank houses and acid resistant gloves when doing inspection on- or harvesting the cells.

Measurement overview

There were 3 shifts per day: the morning shift (06:00 – 14:00), afternoon shift (14:00 – 22:00) and the night shift (22:00 – 06:00). Monitoring was done during the morning and afternoon shifts. Data were pooled as there was no difference in sulphuric acid levels between the two shifts. The two tank houses were monitored on separate days and two workers' sulphuric acid mist exposures and skin conditions were monitored per shift. Two respiratory sulphuric acid mist samples were taken per shift per worker, one from 06:30 – 08:45 and one from 09:30 – 12:45 for the morning shift, one from 14:30 – 16:45 and one from 17:30 – 20:45 for the afternoon shift.

Periods were selected based on the fact that workers have a 15 minute break at 09:00, and a 30 minute break for lunch at 12:00, after which their work shift ends and they head to the change houses. During the lunch shift these times would be 17:00 and 21:00. To successfully acclimatise the workers to the control room temperatures so that accurate skin hydration and TEWL measurements can be acquired, the workers were asked to stop working 15 minutes before their breaks started. The sorbent tubes used to monitor sulphuric acid mist levels were switched with new tubes whenever the workers had their skin condition measured. This was done to determine the variability of sulphuric acid mist concentration between the two sampling periods, and then correlated with changes of the skin surface pH during the same periods, if any. This was done to give a clearer view on what effect a rise or fall of sulphuric acid mist concentrations, due to changes in work procedures, would have on the skin surface pH. These findings were then correlated with TEWL and hydration values to see if they had any effect on the skin barrier function. Therefore, the airborne concentrations of sulphuric acid mists were correlated with the degree of damage to the skin barrier.

Employees were briefed on the scope of the project (purpose of the study and the monitoring procedure) by means of a PowerPoint presentation during the pre-shift meetings and volunteers gave written consent before being sampled. Shift supervisors, who are proficient in both English and the local language Setswana, translated instructions to the workers.

Skin variable measurement

Skin surface pH, -hydration and transepidermal water loss (TEWL) measurements were taken to determine the skin's surface pH due to sulphuric acid mist exposure as well as the damage the mists may have inflicted on the skin. Qualitative swab tests were performed to determine the presence of nickel and copper on workers' skin. If high TEWL values were obtained and nickel or copper were present on the skin, it could be deduced that the rate of percutaneous absorption of these two ions and their salts might be greatly increased.

Instruments used:

- TEWL Meter – Delfin® Vapometer (SN: SWL-4422)
- Derma-Unit SSC3 Corneometer® (SN: 09299470)
- Derma-Unit SSC3 Skin-pH-meter® probe (SN: 11111560)
- Kestrel 4000 (SN: 637072)

Procedure

The maximum risk employee could not be identified, therefore OESSM was used to determine the size of the Similar Exposure Group (SEG).

Members of the SEG completed the skin questionnaires provided (Skin questionnaires obtained from Dalgard *et al.* (2003) and the Nordic Skin Questionnaire (Short Version) (Susitaival *et al.,* 2003) on the day their respiratory samples and skin measurements were taken. The Dalgard questionnaire was given in English and Setswana and the Nordic questionnaire only in English. As was the case with the PowerPoint presentation, the shift supervisor was available for translation.

The Dalgard questions were scored on a four point scale, namely (1: no, 2: yes, a little, 3: yes, quite a lot and 4: yes, very much). These scores were then calculated, and according to the authors, subjects with scores of 1.3 and higher have a higher risk of developing skin diseases.

The Nordic skin questionnaire is used to monitor the prevalence of skin diseases, and was used in this study to ensure that all members of the SEG were as homogenous as possible.

Measurement of skin surface pH, hydration and TEWL

Three measurements were taken during each shift, once before the shift started, once during the shift before the tea break and once at the end of the shift before the employees left for the change house.

Calibration of skin measurement instruments

Delfin® Vapometer

The Delfin® Vapometer used was within the proper calibration period which is once per year.

The Skin-pH-meter® and Corneometer® were calibrated according to the manufacturer's instructions (Courage & Khazaka electronic GmbH, 2008).

Skin-pH-meter®

Firstly the potassium chloride (KCl) level of the pH probe was checked to make sure it was at an acceptable level. The meter was then calibrated using two buffer solutions, one with a pH level of 4.0 and one with a pH level of 7.0. During calibration the pH sensor was cleaned with distilled water and then dipped in the solution with a pH of 7.0 for 20 seconds until a stable reading was displayed. The sensor was cleaned with distilled water again and dipped in the solution with a pH of 4.0 for 20 seconds. The pH sensor was then calibrated. The calibration process was performed once a day before the morning shift started.

Corneometer®

A plastic plate used for calibration was prepared by soaking an absorbent pad with special calibration fluid and covering it with a piece of film, cut in such a way that the hydration probe did not come into contact with the calibration fluid. The hydration probe was pressed onto the film until a stable reading of 20 ± 5 a.u. was obtained. This film was then removed and the probe was pressed onto the soaked pad until a stable reading of 120 ± 5 a.u. was obtained. The Corneometer® was then calibrated. This was done once a day before the morning shift started.

The three skin variables were measured on six different body areas, which were then divided into two groups, namely the covered areas which included the areas that are covered by gloves and overalls and the exposed areas which included the areas that are not protected from sulphuric acid mists by protective clothing or gloves.

The covered areas comprised of the palm of the hand, the back of the hand and the inner forearm areas, while the exposed areas comprised of the forehead, cheek and neck areas (see Figures 1 and 2).

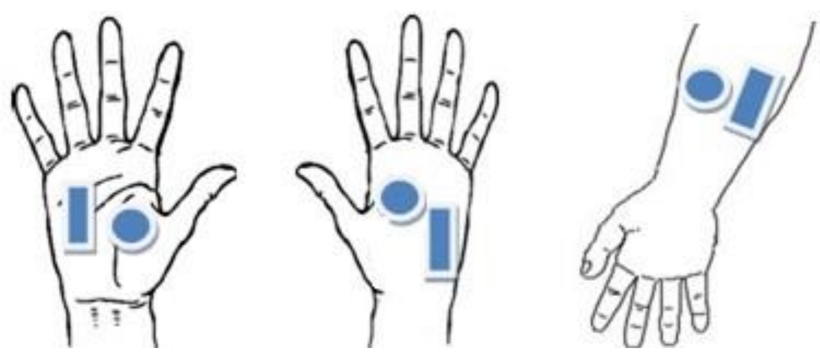

Figure 1: Measurement of the covered areas*.

*** The circular shaded area indicates where hydration, TEWL and skin surface pH measurements were taken. The rectangular, 10 cm^2 shaded area indicates where the qualitative spot test was done.**

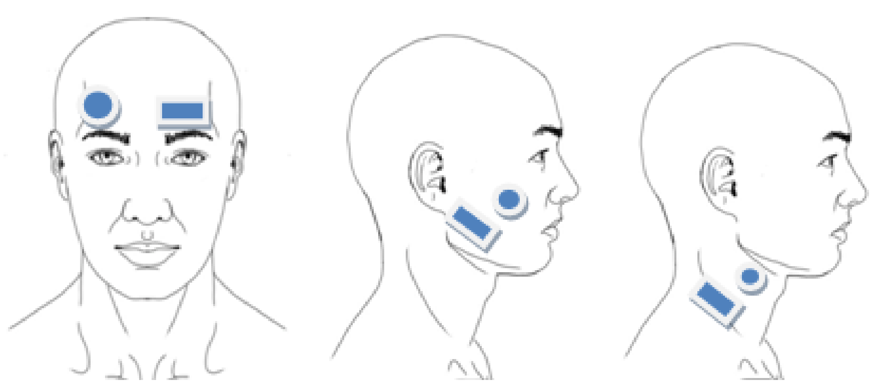

Figure 2: Measurement of the exposed areas*.

*** The circular shaded area indicates where hydration, TEWL and skin surface pH measurements were taken. The rectangular, 10 cm^2 shaded area indicates where the qualitative spot test was done.**

Skin variables were measured on the worker's dominant hands. Skin measurements on the forehead were done 2 cm above the dominant side's eye, and the qualitative spot test was done above the other eye.

Three skin surface pH and –hydration measurements were taken on all six areas to acquire an accurate average reading, while only two TEWL readings were taken due to time constraints.

To avoid false positive TEWL values, certain measures were taken. Test subjects gathered in the tank house control room where the environmental temperature and humidity was measured with the Kestrel 4000. Ambient air temperature was controlled by means of an air conditioning unit. If humidity levels fell outside the 40 – 60% range, no further samples were taken during that shift. Before measurements with the pH-, hydration- and TEWL meters were taken, the subjects had to acclimatise to the room temperature i.e. stop sweating. They were given a minimum of 15 minutes for this process.

Before the initial measurements were taken, i.e. before the work shift started, the workers were asked to complete two skin questionnaires, namely the Dalgard- and Nordic (short) questionnaires. One of the most important questions was whether or not these workers use skin care products during or after work. The members of the SEG comprised only of employees that did not use skin care products.

Workers were asked not to wash their hands or eat or drink any hot drinks before the measurements were completed. The skin measurements were done before the qualitative spot test to avoid any possible effect the moisture from the wet wipe could have had on the skin measurements readings. Skin hydration, skin surface pH and TEWL measurements were taken intermittently to speed up the measurement process.

TEWL measurements were taken to determine the level of skin barrier deterioration. Hydration levels were measured to determine the overall health of the skin. Skin surface pH measurements were taken to determine if skin surface pH values were still within healthy ranges. Data from all three variables were correlated with the sulphuric acid mist concentrations to determine the effect on the skin barrier function.

Vapometer

No accurate index could be found for the Vapometer, although values between 13 – 15 $g/m^2/h$ are accepted as normal for Africans according to Singh *et al.* (2000). Values of >15 $g/m^2/h$ indicate heavy water loss through the stratum corneum.

Corneometer®

The readings on the SSC3 Corneometer® are given in arbitrary units. The following index is found in the SSC3's manual (Courage & Khazaka electronic GmbH, 2008).

Table 1: SSC3 Corneometer® Index Values given in arbitrary units (a.u.).

Hydration Level	Interpretation	Skin Barrier Function
<30	Very dry	Very Poor
30 – 45	Dry	Poor
>45	Sufficiently Hydrated	Normal

<u>Skin surface sampling with wet wipes</u>

The areas that were measured were the same as the areas mentioned above as they were suspected to be the areas on the body with the highest exposure to the substances being measured. Measurements were also taken at the same times, i.e. before the work shift started, before the break and before lunch.

This measurement method was based on NIOSH's method for sampling with Ghostwipes™, method 9102, which proceeded as follows (Figure 3); the wet wipe was wiped across the skin in a ± 10 cm^2 area in a horizontal S-pattern. The wet wipe was folded inward as required by the method and the same area of the wet wipe was used to measure the same ± 10 cm^2 area again, only in a perpendicular pattern to the first measurement, i.e. a vertical S-pattern. Once again the wet wipe was folded inward, and the wet wipe was used on the same area for a third time, once again with the direction of sampling perpendicular to the second measurement, i.e. the same as the first measurement (NIOSH, 2003).

Latex gloves were worn with each of the measurements, and changed after every measurement to avoid contamination.

Reagents were prepared by the researcher in their respective concentrations in a controlled laboratory environment and placed in spray bottles.

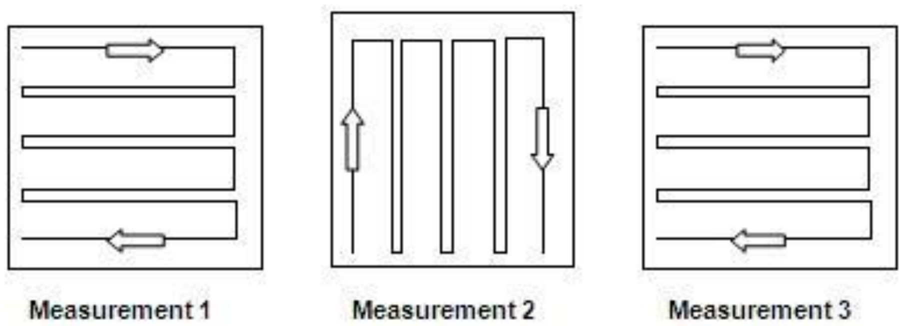

Figure 3: NIOSH method 9102 ghost wipe method (NIOSH, 2003)

<u>Qualitative test for nickel</u>

The reagents used for the qualitative test for nickel are the same as used in DELASCO®'s Self-Help Spot Test for Nickel.

Reagents for the nickel test:

- 1% Dimethylglyoxime solution;
- 10% Ammonium hydroxide solution.

The wet wipe was held by hand and sprayed with the 1% dimethylglyoxime solution. After a few seconds the wet wipe was sprayed with the 10% Ammonium hydroxide solution.

If a pink-red colour was obtained, the presence of nickel on the skin was confirmed.

Figure 4: Swab taken on a piece of nickel sheeting, the pink colour reaction shows a positive result.

Qualitative test for copper

The reagents used for the qualitative test for copper were adjusted from the method used to test the copper content of soil, as used by West (1945).

Reagents for the copper test:

- 20% Malonic Acid solution;
- 1% Dithiooxamide (a.k.a. Rubeanic Acid) + 95% Ethanol.

The wet wipe was held by hand and sprayed with the 20% malonic acid solution. After a few seconds the wipe was sprayed with the 1% dithiooxamide, 95% ethanol solution.

If a dark green colour was obtained, the presence of copper on the skin was confirmed.

Figure 5: Swab taken on a piece of copper sheeting, the dark green colour reaction shows a positive result.

Respiratory sampling

Seeing as though the sulphuric acid mist concentrations needed to be determined as a reference to determine the effect of the mists on the skin barrier function, personal monitoring was done on the same workers that the skin measurements were performed on using NIOSH Method 7903 (NIOSH, 2003).

For this method, a two part SKC silica gel sorbent tube, 7 x 110 mm (Cat no. 226-10-03), was used and placed in a SKC sorbent tube holder (Cat no. 222-3-1) and attached to a Gilian GilAir3 sampling pump (SN: 20120402023 & 20110101006) with attached low-flow unit with the flow rate set to 0.25 - 0.5 l/min using a Gilibrator (SN: 20069-S). In this study air flow rates were set at 0.326 ± 0.007 l/min to ensure that at least half of the maximum allowable volume of air, namely 100 l, was sampled.

Two samples were taken per worker per shift of 2.5 to 3 hours. The samples were sent for analysis by a SANAS accredited laboratory by means of ion chromatography.

Quality control

One sorbent tube from each batch was used as a reference seeing as the tubes are pre-loaded with sulphur.

Step 1: Pre-sampling calibrations

- Gilian air sampling pumps calibrated to 0.2-0.5 l/min.
- Hydration- and skin surface pH meter calibrated.

↓

Step 2: Pre-sampling

- Two workers asked to volunteer.
- Workers moved to control room (controlled temperature and humidity).
- Workers filled in two skin questionnaires and consent forms while acclimatising.

↓

Step 3: Sampling Phase 1

- Three skin variables measured on both workers.
- Gilian pump attached to workers' overalls, sorbent tube placed in respiratory zone on workers' dominant side.
- Workers asked to return to control room 15 minutes before tea break starts.

↓

Step 4: Sampling Phase 2

- Gilian pumps post flow calibrated and recalibrated for phase 2 sampling, and
- Sorbent tubes sealed and switched with new tubes while workers acclimatize for 15 minutes.
- Three skin variables measured on the workers.
- Gilian pumps re-attached to workers.
- Workers asked to return to control room 15 minutes before lunch break starts.
- Sorbent tubes stored in refrigerator in Occupational Hygiene lab.

↓

Step 5: End of sampling

- Gilian pumps post flow calibrated, sorbent tubes removed and sealed.
- Three skin variables measured on both workers.
- Gilian pumps placed on charge and sorbent tubes stored in refrigerator in Occupational Hygiene lab.

Figure 6: Sampling quality control checklist.

Data processing

Skin variable- and sulphuric acid concentration results were analysed to obtain Spearman correlation coefficients between the acid concentration and the three skin variables. A p-value of ≤ 0.05 indicated a significant correlation, while an r-value of ≥ 0.8 was seen as a strong correlation and 0.5-0.8 as an average correlation.

If a negative result was acquired with the qualitative nickel and copper tests a zero value was assigned whereas a one was assigned to a positive result. Results were statistically analysed using Statistica 11 (Statsoft Inc., 2012) and figures were drawn using GraphPad Prism 5.03 (GraphPad Software Inc., 2009).

Ethical aspects

All test subjects volunteered to take part in this study, signing informed consent forms before any monitoring was performed. Test subjects did not receive any form of remuneration or incentive to partake, and all results were kept confidential and only shared with the workers themselves and the Occupational Hygiene Department of the refinery, to be used for the recommendation of further control measure implementation.

3.3 Results

The results of this study were presented in tables and figures and consequently discussed. Outliers were not used during data processing. The upper and lower quartiles were calculated, and any values not within these quartiles were seen as outliers.

Skin surface measurement averages and standard deviations are shown in a lined grouped plot graphs rather than the more frequently used whisker plot. This was done to simplify comparing the difference in values found on the measurement areas, as well as how the values changed during the work shift.

TEWL

Mean TEWL values for all measurement areas on the copper tank house workers decreased towards the tea break, and then increased again towards the end of the shift. In every case the end of shift values increased to levels higher than those seen at the before shift measurement time, except for the forehead, remaining constant with values of 25.3 ± 8.0 g/m^2/h at the tea break and 25.3 ± 7.3 g/m^2/h at the end of the shift.

For the nickel tank house workers the results show the same pattern, but with only the back of hand and cheek areas shower higher TEWL values at the end of the shift than before the shift started. The palm, inner forearm, forehead and neck areas show lower TEWL values at the end of the shift than at the beginning of the shift.

Linear regression analyses were conducted and none of these findings are statistically significant, due to the large deviation seen in the TEWL values.

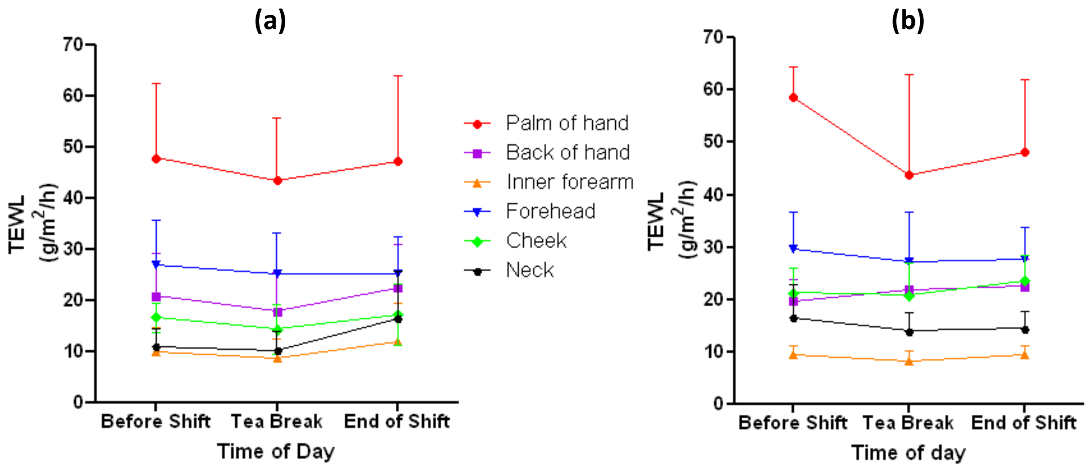

Figure 7: Average values of TEWL measured during three measuring intervals on workers in the copper- (a) and nickel (b) tank houses*.

*** The averages and standard deviations were calculated with a minimum of four values for both tank houses and a maximum of eleven for the copper tank house and eight for the nickel tank house.**

The before shift forehead TEWL readings showed TEWL significantly higher in the nickel tank house workers than the copper tank house workers (p=0.047).

It is clear in the two figures that the palm of the hand showed the highest TEWL values, with mean values at 47.9 ± 14.6 g/m^2/h for the copper tank house workers and 58.6 ± 5.8 g/m^2/h for the nickel tank house workers. As seen in the literature, any value above 15 g/m^2/h indicates heavy water loss through the skin and a compromised skin barrier function.

Hydration

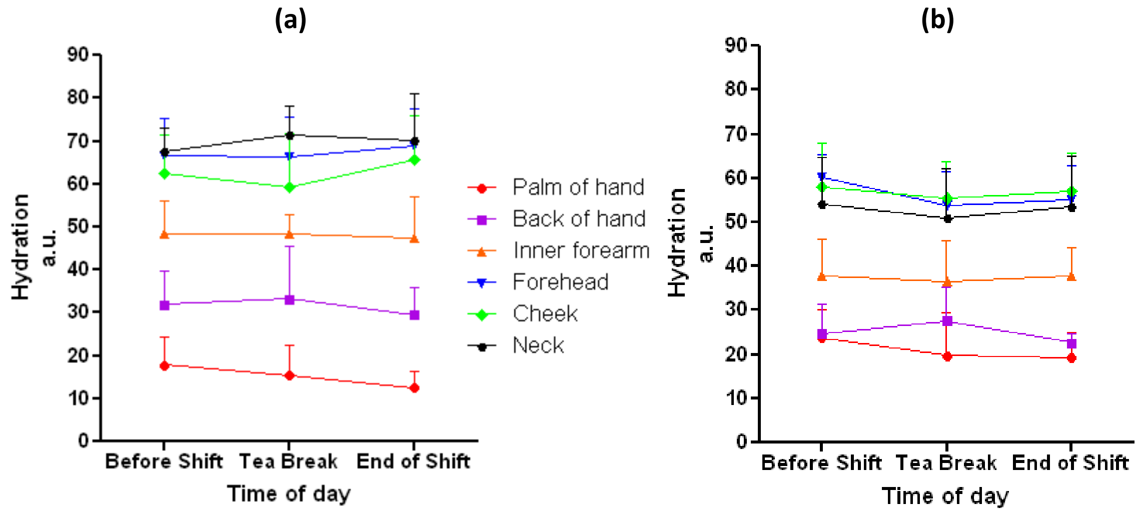

Figure 8: Average values of skin hydration measured during three measuring intervals on workers in the copper- (a) and the nickel (b) tank houses*.

*** The averages and standard deviations were calculated with a minimum of eight values for both tank houses and a maximum of thirty-three for the copper tank house and twenty four for the nickel tank house.**

Mean hydration values for the palm of hand on both tank house workers showed a steady decrease in hydration towards the end of the shift. Interestingly, the back of hand areas on both tank house workers also share a pattern, that increased towards the tea break, and decreased towards the end of the shift to values lower than the before shift values, although no statistical significance could be found.

The before shift neck hydration readings showed significantly higher readings on the copper tank house workers than the nickel tank house workers (p=0.022).

As was stated above, nickel tank house workers showed the highest TEWL values on all body areas, and in agreement with literature the hydration values for the corresponding body areas were also lower (Darlenski *et al.*, 2009) in nickel tank house workers than in the copper tank house workers. This was the case for all body areas except for the palm of hand area, although it was not statistically significant.

Skin surface pH

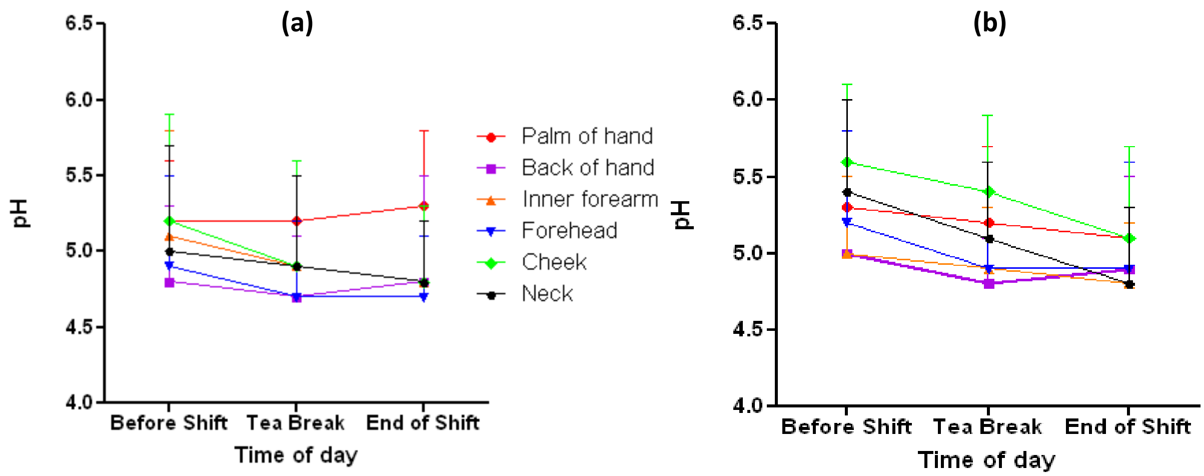

Figure 9: Average values of skin surface pH measured during three measuring intervals on workers in the copper- (a) and nickel (b) tank houses*.

*** The averages and standard deviations were calculated with a minimum of eight values for both tank houses and a maximum of thirty-three for the copper tank house and twenty four for the nickel tank house.**

The copper- and nickel tank house workers showed very little difference in the skin surface pH levels measured in the covered measurement areas, but when comparing the exposed areas, it was clear that the skin surface pH on the copper tank house workers was 0.4 units lower at the beginning of the shift on all three areas, 0.2 lower for the forehead and neck areas with the difference of 0.5 units between the cheek areas. Towards the end of the shift copper tank house workers showed pH values 0.2 units lower than nickel tank house workers in figure 9, but no statistical difference could be found.

In the copper tank house, all body areas showed a decrease in skin surface pH from the beginning of the shift until the tea break, with the exception of the palm- and back of hand areas. For the inner forearm, the cheek and the neck areas, the skin surface pH continued decreasing during the tea break to end of shift monitoring period, but for the palm of hand and back of hand areas, the pH increased towards the end of the shift.

In the nickel tank house, all body areas again showed a decrease in skin surface pH from the beginning of the shift until the tea time break, but only the back of the hand area showed an increase in surface pH towards the end of the shift, while the skin surface pH for all other areas continued to decrease.

Personal respiratory sampling

In order to determine what effect, if any, the sulphuric acid mist in the tank house environment could have on the workers' skin barrier function, the airborne concentration of these mists had to be determined.

Table 2: TWA values for airborne sulphuric acid concentrations in both tank houses.

	TWA Airborne sulphuric acid concentration (mg/m^3)		
Tank house	**Before shift – Tea break**	**Tea break – End of shift**	**TWA-OEL**
Copper tank house	0.024 ± 0.026	0.11 ± 0.146	1
Nickel tank house	0.013 ± 0.008	0.031 ± 0.031	

Values above indicate the mean sulphuric acid mist concentration and standard deviation per tank house for each of the monitoring shifts. Occupational exposure limits to airborne sulphuric acid are set as 1mg/m^3 in both the Regulations for Hazardous Chemical Substances, 1995, of the Occupational Health and Safety Act No. 85 of 1993, and the OEL prescribed in Schedule 22.9(2)(a) of the Regulations of the Mine Health and Safety Act No. 29 of 1996.

Skin questionnaires

According to the authors of the Dalgard skin questionnaire, subjects with scores of 1.3 and higher have a higher risk of developing skin diseases (Dalgard *et al.,* 2003).

The average Dalgard score for copper tank house workers was 1.05 ± 0.08 with only two of the eleven subjects reporting a score of 1.2. Four of the eleven workers reported with one or more of the following, namely itchy skin (one worker) which appeared a week ago, scaly skin (one worker) which appeared more than six months ago, itchy rash on hands (one worker) and warts (one worker) which appeared more than six months ago.

For the nickel tank house workers, the Dalgard score was higher at 1.14 ± 0.12 with four of the eight test subjects scoring 1.2 and one scoring a 1.3. Four of the eight workers reported having itchy skin and pimples, while two workers complained of an itchy rash on their hands with one worker complaining of a rash on his face. All complaints of itchy skin started a month ago, although some workers said they have been struggling with itchy skin for more than six months. Pimples were only seen on younger employees.

All workers said they normally used some form of skin cream when they arrive at work after changing into their overalls, and at the end of the work shift after they showered. They stopped using these creams for the duration of the study.

Qualitative swabs

Throughout the working shift no copper tank house workers tested positive for the presence of copper on the skin. Nickel tank house workers however tested negative before the shift started, but all showed the presence of nickel on all six measuring areas during tea break and end of shift measurements.

Correlations between sulphuric acid mist and skin variables

The Spearman rank coefficient of determination i.e. the R_2 value was calculated to determine the monotone relationship between two data sets. The individual values were used for all measurement areas for every variable (TEWL, hydration and pH) over the three monitoring times (before shift, tea break and end of shift) and compared to the airborne sulphuric acid mist concentrations. Tables 3 and 4 therefore represent the correlation values for the average sulphuric acid concentrations over the three monitoring times to the three skin variables. The individual values were used in this table to give the most accurate representation of the inter-variability seen in workers' skin. This, and the large variability in sulphuric acid mist concentrations that were measured, makes it difficult to find statistically meaningful correlations, but the more significant correlations are discussed below and their individual results will be depicted in figures.

For the percentage changes graphs that follow, the above mentioned areas were chosen, one for the exposed group and one for the covered group.

Table 3: Spearman rank correlation coefficients of airborne sulphuric acid mist concentrations with TEWL, skin hydration and pH of different areas of the exposed skin of workers in the copper tank house.

Skin Variable	Measurement Area	Slope	R_2-value	r-value	p-value
TEWL	Palm of hand	0.089 ± 0.043	0.04	0.200	0.263
	Back of hand	0.053 ± 0.028	0.005	0.071	0.691
	Inner forearm	0.04 ± 0.025	0.0002	0.014	0.932
	Forehead	0.038 ± 0.03	0.0011	0.033	0.854
	Cheek	0.035 ± 0.037	0.0024	0.049	0.789
	Neck	0.036 ± 0.037	0.0017	0.041	0.814
Hydration	Palm of hand	0.063 ± 0.031	0.155	0.394	0.49
	Back of hand	0.041 ± 0.05	0.00014	0.012	0.94
	Inner forearm	0.116 ± 0.114	0.0128	0.113	0.529
	Forehead	-0.102 ± 0.131	0.039	0.197	0.267
	Cheek	-0.0019 ± 0.102	0.0067	0.082	0.648
	Neck	-0.009 ± 0.15	0.004	0.063	0.723
pH	Palm of hand	-0.253 ± 0.225	0.054	0.232	0.194
	Back of hand	0.061 ± 0.158	0.0003	0.017	0.915
	Inner forearm	0.007 ± 0.155	0.002	0.045	0.814
	Forehead	-0.102 ± 0.157	0.027	0.164	0.357
	Cheek	0.232 ± 0.131	0.063	0.251	0.16
	Neck	0.199 ± 0.141	0.038	0.195	0.278

For copper tank house workers (Table 3), TEWL showed a positive slope for both the palm and forehead areas when compared to sulphuric acid mist exposure, meaning that as sulphuric acid mist levels increased, so did TEWL. However due to the large variation seen in TEWL and sulphuric acid mist exposure, no significant correlation could be found.

As for hydration, the palm showed a positive slope, with the forehead showing a negative slope, meaning that as the sulphuric acid mist levels increased, skin hydration decreased. For both the palm and forehead areas, a negative slope is seen when comparing skin surface pH values with the sulphuric acid mist concentrations. Even though this yielded the expected result, that skin surface pH would decrease with an increase in sulphuric acid mist, no meaningful correlation was found.

Table 4: Spearman rank correlation coefficients of airborne sulphuric acid mist concentrations with TEWL, skin hydration and pH of different areas of the exposed skin of workers in the nickel tank house.

Skin Variable	Measurement Area	Slope	R_2-value	r-value	p-value
TEWL	Palm of hand	0.011 ± 0.008	0.056	0.237	0.326
	Back of hand	-0.031 ± 0.017	0.253	0.503	0.012
	Inner forearm	0.015 ± 0.025	0.0005	0.022	0.973
	Forehead	-0.027 ± 0.012	0.349	0.591	0.002
	Cheek	0.016 ± 0.014	0.0003	0.017	0.931
	Neck	0.023 ± 0.016	0.123	0.351	0.605
Hydration	Palm of hand	0.019 ± 0.013	0.005	0.071	0.737
	Back of hand	0.033 ± 0.019	0.042	0.205	0.334
	Inner forearm	0.022 ± 0.023	0.0054	0.073	0.733
	Forehead	0.033 ± 0.037	0.011	0.105	0.619
	Cheek	0.0011 ± 0.031	0.009	0.095	0.661
	Neck	0.016 ± 0.024	0.0001	0.010	0.962
pH	Palm of hand	0.01 ± 0.058	0.0002	0.014	0.943
	Back of hand	0.021 ± 0.052	0.0008	0.028	0.896
	Inner forearm	0.097 ± 0.055	0.093	0.305	0.146
	Forehead	0.073 ± 0.036	0.104	0.322	0.123
	Cheek	0.145 ± 0.037	0.355	0.596	0.002
	Neck	0.127 ± 0.036	0.308	0.555	0.004

As can be seen in Table 2, workers in both tank houses experienced sulphuric acid mist exposure of 10 – 50% of the OEL-TWA (max = 0.452 mg/m^3). Due to this fact, and because of the large variation seen in measured sulphuric acid values, no statistically significant correlation was found between the sulphuric acid exposure and any of the three skin variables in copper tank house workers.

For nickel tank house workers (Table 4), only the back of hand and forehead areas showed significant changes in TEWL ($p = 0.012$ and 0.002 respectively) brought on by sulphuric acid exposure.

Other than the copper tank house, the relationship between TEWL and sulphuric acid exposure yielded a negative slope. When comparing skin hydration to sulphuric acid mist exposure, both the back of hand and forehead areas show a positive slope, indicating that skin hydration increased together with sulphuric acid exposure. Skin surface pH shows a positive slope when compared to sulphuric acid exposure, the opposite of what was seen in the copper tank house. A significant change was also caused in the skin surface pH by the sulphuric acid in the cheek and neck areas, two areas belonging to the exposed areas.

Percentage changes

In order to determine the effect the airborne sulphuric acid mist had on the skin barrier function, the percentage changes of the acid concentration and TEWL were calculated and correlated.

No meaningful correlations were found, the strongest correlations shown by the back of hand area from the tea break to the end of the shift ($r = -0.232$, $p = 0.889$).

3.4 Discussion

The lower sulphuric acid mist concentration in the nickel tank house showed that the combination of anode bags and electrolysis bath covers are a more effective control measure than the polypropylene beads used in the copper tank house, although exposure in both tank houses was relatively low when compared to the OEL. Both tank house cells have the same ventilation measures installed, namely extraction hoods inside the cells to minimise employee exposure.

Ventilation measures are constantly being revised and improved due to the high probability that the OEL will be lowered during the next revision of the hazardous chemical substances regulations (Pavlides *et al.,* 2008).

The nickel tank house workers showed higher TEWL values, as well as lower hydration values than the copper tank house workers. It cannot be determined whether this is due to the sulphuric acid alone; seeing as no copper was found on the copper tank house workers' skin, while the nickel tank house workers all showed the presence of nickel on the skin, a well-known skin sensitiser (Table 4) (Du Plessis *et al.,* 2010).

The palms of both tank house worker groups showed the highest TEWL values. This can be attributed to a number of factors. Firstly, these employees are manual labourers, meaning the skin on the palm of the hand is subjected to more mechanical friction than the average person's. This wear and tear can lead to physical damage of the stratum corneum, leading to an increase in TEWL and a decrease in hydration, as can be seen by the low hydration values in Figure 8. This is supported by the fact that the inner forearm showed the lowest TEWL values, due to the fact that the forearm is less prone to mechanical friction, and is covered by the acid resistant overall.

Regardless of the fact that the workers were familiarised with the methods and instruments used, the white coat effect was still clearly visible whenever monitoring was done. The majority of the workers believed, despite being told otherwise, that these instruments used needles to prick the skin and draw blood. This could have led to increased perspiration, especially on the palm of the hand, which could have led to falsely high values during the before shift measurement. During the tea break measurements the workers were more comfortable with the instruments after having seen that they are non-invasive, but the end of shift measurements TEWL values are still the highest for the palm of hand area due to the manual labour being performed by hand, as stated earlier. Corrosive damage could also have been done to the palm skin due to compromised PPE integrity and incorrect use.

The effect of sweat on the Vapometer used to measure TEWL well documented, so it is likely that the reading was influenced by perspiration. This idea is supported by the fact that the second highest TEWL values were seen on the forehead, another area of the body prone to perspiration during times of stress.

As explained in the literature (Filon *et al.,* 2009), the effect of sweat also has to be taken into account, seeing as increased physical activity, such as during manual labour, will lead to an increase in perspiration and a decrease in the skin surface pH. This will ionise the sulphuric acid, copper- and nickel present on the workers' skin, which may increase permeability for metallic ions (Larese *et al.,* 2007) and acids (Li *et al.,* 2012). This is supported by the fact that the second and third highest TEWL values were seen on the forehead and back of hand areas. During physical labour sweat will accumulate on the forehead, and due to the fact that these workers wear gloves during their work shift, the palm and back of the hand areas would have been covered in a layer of sweat.

The wearing of gloves also leads to perspiration on the palm- and back of hand areas. If the breakthrough limit on these gloves has been exceeded, sulphuric acid could then penetrate the glove and come into contact with the worker's skin. This would entrap acid inside the gloves (De Craecker *et al.,* 2008), and the low pH of the sulphuric acid, combined with the already low pH of the skin caused by the physical activity, could lead to skin damage. It is unknown in this study whether this occurred, as no skin surface sampling was done to determine the presence or concentration of sulphuric acid. If any metal ions were present on the skin as well, as is the case with the nickel tank house workers, these metals could then be ionised in the low pH solution on the skin surface, leading to the absorption of these ions into the skin (Larese *et al.,* 2007; Filon *et al.,* 2009), leading to further skin damage. These ions could have come into contact with the skin by either penetrating old worn gloves or by the incorrect use of PPE. Workers therefore have to stick to a strict regimen of replacing their gloves regularly and attending training.

As mentioned in the TEWL section of the results, the palm of hand skin hydration values showed the lowest averages in both tank houses due to excessive water loss indicated by the high TEWL values. It is clear that the skin in the facial area (exposed) shows higher hydration values than the arm and hand (covered). This can be attributed to the skin's physiological differences seen in different parts of the body, such as the lamellar lipids in the skin in the facial area being more densely packed, and the larger cells creating a larger diffusion path (Rawlings and Harding, 2004).

As was stated above, nickel tank house workers showed the highest TEWL values on all body areas, and as stated in the literature, the corresponding body areas also show lower hydration values in nickel tank house workers than in the copper tank house workers.

The only statistically significant difference was seen in the before shift neck measurements, with copper tank house workers showing higher values. When comparing the graphs in Figure 2 the palm of hand areas for both tank house workers showed levels lower than 30, indicating very dry skin. This is also the case for the back of hand values for the nickel tank house workers, but the copper tank house workers showed values in the 30 – 45 range, i.e. dry skin. For both tank house workers the exposed measuring areas all showed hydration values of 50 and higher, indicating that the skin is sufficiently moisturised. This can be attributed to the physiological differences seen in the skin of the hand and skin of the face, the latter being thicker with more densely packed lipids.

As stated in the results there is no real difference in skin surface pH values in the covered areas, however it is clear that for the exposed areas the copper tank house workers showed values lower than the nickel tank house workers. Again, the sulphuric acid mist concentrations in the copper tank house were much higher than levels measured in the nickel tank house. This is most likely why the copper tank house workers showed a lower skin surface pH than the nickel tank house workers in the exposed body areas, although no statistical significance could be found. A possibility exists that the gloves the workers were wearing offered adequate protection against the concentrations of acid mist encountered in their respective working environments.

It is clear that nickel tank house workers showed higher Dalgard scores on average. This can be attributed to the fact that nickel is a strong sensitiser, and has been well documented in the past to lead to allergic dermatitis and itchy, rashy skin (Filon *et al.,* 2009).

Only the nickel tank house workers complained of having pimples on their face, and upon closer inspection it was seen that it was the four workers in their twenties that lodged these complaints. It is unclear then whether these pimples were caused by workplace exposure to certain substances, or because these workers are still at an age where pimples are still quite common.

No statistically meaningful correlations were seen in the copper tank house workers, however in the nickel tank house the back of hand ($r = 0.503$, $p = 0.012$) and forehead ($r = 0.591$, $p = 0.002$) areas both showed an average negative correlation, indicating that as the sulphuric acid mist concentration increased, TEWL decreased. Sulphuric acid mist levels may have lowered the skin pH to such levels that desquamation was optimized (Harding *et al.,* 2000). As the employees were only exposed to low levels of sulphuric acid mist in the tank house (max = 0.084 mg/m^3), higher concentrations may have led to corrosive skin damage.

In the nickel tank house, the cheek ($r = 0.596$, $p = 0.002$) and neck ($r = 0.555$, $p = 0.004$) areas showed average positive correlations between sulphuric acid concentration and skin surface pH. This may be because employees continued using skin creams during the study contrary to what was stated in the skin questionnaire, which raised their skin surface pH, or the soap the workers use in the change house contain substances which also raise the skin surface pH.

Quantitative tests were not carried out in this study to determine the concentration of acid and metals present on the skin, so their influence on the results of this study is unknown. Qualitative test however were performed; these showed that in the copper tank house no copper was detected on the workers' skin from the beginning to the end of the shift. The nickel tank house workers however all tested positive for the presence of nickel on the skin during tea break and end of sift measurements.

It is mandatory for these workers to wear gloves and overalls whenever entering the tank house, so breakthrough could have occurred, leading to the nickel being present on the exposed and covered areas of the skin. Another possibility is that workers use items such as taps and door handles while still wearing their gloves, followed by another worker using the same item without wearing his gloves, thereby transferring the nickel left behind on the items to that worker's skin (Du Plessis *et al.,* 2010).

As nickel is a sensitising agent, emphasis will have to be placed on the prevention of second hand transfer from object to worker. The easiest way to implement this will be to mount signage in the tank house prohibiting the wearing of gloves anywhere outside the tank house, and not in the tea room or control room. As nickel was found to be present on the skin, it could be on the overalls as well (Du Plessis *et al.,* 2010). These overalls will have to be washed after every use, and the workers must hand their overalls in at the laundry before they shower, so as to not be contaminated with nickel when they leave the change house.

Workers in both tank houses wore latex gloves while in the tank house area. Previous studies have shown that 17 – 36% of workers present with a latex allergy (Edlich *et al.,* 2003), seeing as latex is also a sensitising agent (Bousquet *et al.,* 2006).

3.5 Conclusion

The results of this study showed no clear indication of the effect sulphuric acid mist might have on the human skin barrier function. What was observed was that workers exposed to nickel have skin that is less healthy than people exposed to copper in the working environment based on the higher TEWL readings. The degree of skin irritation caused by copper is as yet unknown (Hostynek and Maibach, 2004), but nickel and its salts are well known skin sensitisers (Ikarashi *et al.,* 1996; Du Plessis *et al.,* 2010). The additive or synergistic effect sulphuric acid has in this regard cannot be ignored, as the literature states that a lower skin surface pH leads to the ionisation, and therefore possibly increased solubility and absorption, of metallic compounds. That the sulphuric acid mist the workers are exposed to lowers the skin surface pH was clearly seen when comparing the data of the exposed skin areas between the copper and the nickel tank house workers.

Control measures such as PPE and ventilation are already in place, but the importance of leadership cannot be ignored. Workers must be trained on the limitations of PPE and how to handle contaminated items and surfaces, especially in the nickel tank house area. The cleaners must also be reminded to often clean areas easily overlooked, such as door handles and taps, to minimise contamination of the environment with work place health hazards.

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Chapter 4

Conclusion and Recommendations

4.1 Conclusions

The aim of this study was to assess the influence of sulphuric acid mist on the skin barrier function of base metal refinery workers. Personal airborne sulphuric acid mist measurements were taken on workers, as well as measurements of three skin variables, namely TEWL, hydration and skin surface pH, which are internationally approved methods of determining skin barrier function. The protective, or possibly detrimental, effect of PPE was also investigated by dividing the skin measurement areas into two groups, namely a covered group which was covered by PPE such as gloves and overalls, and the exposed group, which had no coverings.

TEWL

In both tank house workers the TEWL values were the highest in the palm of hand area, due to the fact that they are manual labourers and the high values can be attributed to the mechanical friction experienced by the hands as well as the possible contact made with the sulphuric acid if breakthrough occurred. Nickel tank house employees showed higher TEWL values on all six body areas than copper tank house workers. Whether this was caused by the sulphuric acid mist or the nickel these workers are exposed to could not be proven by this study. However, the fact that the two tank houses have the same PPE prescribed and that the copper tank house showed airborne sulphuric acid mist concentrations up to three times higher than those of the nickel tank house, leads the researcher to believe that the higher TEWL values were caused by the confirmed presence of nickel on the skin. Although the back of hand and forehead areas showed average correlations in the nickel tank house workers, only weak correlations were found when comparing the percentage changes of acid mist concentration with TEWL.

Hydration

Skin hydration was the lowest in the palm of hand areas, once again confirming the negative correlation seen between TEWL and skin hydration as stated in the literature.

The nickel tank house workers showed lower hydration values than the copper tank house workers in all areas except for the palm of the hand. As stated above, nickel is a well-known skin sensitiser, leading to the formation of rashes on workers' skin. These rashes lead to the rapid loss of water through the skin, which may explain the very low hydration values seen on nickel tank house workers' skins.

Skin surface pH

The difference in the skin surface pH of the covered area of measurement areas showed no real difference in pH levels, however when comparing the pH levels of the exposed group, the difference between copper tank house workers and nickel tank house workers is clear; copper tank house workers showed pH values of up to 0.4 lower than the nickel tank house workers. This can only be due to the fact that, as stated above, copper tank house workers were exposed to sulphuric acid levels up to three times higher than the levels that nickel tank house workers were exposed to.

The hypothesis of this study was that exposure to sulphuric acid mist will decrease skin surface pH to levels that will increase TEWL and decrease the level of skin hydration, indicating a decrease in the skin barrier function.

The conclusions drawn from the results state that the sulphuric acid mist levels were much lower in the nickel house than the copper tank house, yet overall the TEWL values were higher and hydration values lower for the nickel tank house workers. This is due to the fact that nickel is present on the workers' skin as it was shown to have penetrated their PPE.

The hypothesis is therefore rejected as the sulphuric acid levels were at such a low level that they may not have had an influence on the skin barrier function.

The effect of airborne sulphuric acid mist on the skin barrier function could therefore not be accurately be determined

4.2 Recommendations

To decrease the amount of sulphuric acid the employees are exposed to, adequate control measures will have to be implemented to ensure maximum protection of worker health. Engineering, administrative and PPE control recommendations are as follows:

A maintenance schedule should be drafted and adhered to for the extraction ventilation systems in both tank houses, to ensure optimum performance.

Mount signage in the tank houses stating that no worker is allowed to wear contaminated gloves in areas other than the tank house, especially in the control- and tea room. A schedule should be implemented for workers to acquire new gloves more frequently, before any possible breakthrough occurs. Workers should furthermore be encouraged to wash their hands and faces before touching anything in the control room or tea room. To prevent contamination by touching tap handles, the installation of taps with motion sensors is recommended.

Surfaces, door knobs and taps should be tested for the presence of nickel. Cleaning staff should then be trained on the health dangers of nickel and which areas are contaminated. This way they can effectively clean the area, and remove as much of the contamination as possible.

In the nickel tank house, breakthrough tests can be performed on gloves and overalls to efficiently determine when the employee should replace his PPE. This will ensure the protection of worker health, as well as save unnecessary costs when replacing PPE too soon.

4.3 Limitations

Due to budget constraints the amount of samples that could be taken was limited due to the financial difficulties faced by platinum mines since 2008. The fact that so few samples were taken led to inconsistent results and could have contributed to the weak correlations that were calculated.

The low concentrations of sulphuric acid mist encountered and presence of skin sensitisers, such as nickel, made it difficult to determine the effect of acid mist on the skin barrier function.

4.4 Recommendations for future studies

Due to the vast variability in the way different people's skins can react to physical and chemical stressors, the following recommendations are made for future studies of this kind:

- Include more workers in the SEG than recommended by OESSM, and each member should be monitored repeatedly over a long time period. This could lead to the researcher obtaining more significant results.
- Ideally a study of this kind must be done on a worker that starts working in an area where he will be exposed to sulphuric acid mist for the first time, to accurately determine the effect of the working environment on his skin barrier function.
- Quantitative swab samples should be done on the worker's skin to determine the concentrations of sulphuric acid, copper and nickel that may be present to determine the cause of skin damage, if any.
- A control group should be used, comprising of staff not exposed to sulphuric acid mist. The members of the control group should be the same age, race and gender as the research subjects to determine the effect of acid mist on the three skin variables and the skin barrier function.
- Conduct this study in an area with higher concentrations of airborne sulphuric acid mist and the absence of substances that could also adverse the skin barrier function.

Annexure A: Dalgard skin questionnaire

PERSONAL DATA SHEET		
Name: ______________	**SAP Nr:** _____________________	**Subject Nr:** _______
Age: _______	**Section:** _____________________	**Date:** _________________
Gender: M / F	**Position:** _____________________	**Numbers of years:** _____
Race: B / W / C / I	**Dominant hand:** L / R	**Smoking:** Yes/No

RESULT SHEET : SKIN QUESTIONNAIRE

During the last week, have you had any of the following complaints?
Mo bekeng e e fetileng, a o kile wa nna le ngwe ya dingongorego tse?

	1 **No** ***Nnyaa***	**2** **Yes, a little** ***Ee, go le gonnye***	**3** **Yes, quit a lot** ***Ee, gantsi***	**4** **Yes, very much *Ee, gantsi thata***
1. Itchy skin (jeuk) *Go babelwa ga letlalo*				
2. Dry/sore rash (droog/seer uitslag) *Boswata bo bo omeletseng/botlhoko*				
3. Scaly skin (afskilfer vel) *Letlalo le le obogang*				
4. Itchy rash on your hands (jeuk uitslag) *Boswata bo bo babelang mo diatleng*				
5. Pimples (puisies) *Dipeise*				
6. Other rashes on your face (uitslag) *Baswata mo sefatlhegong*				
7. Warts (vraatjies) *Diso/dokgoto*				
8. Troublesome sweating (sweet) *Go fufulelwa thata*				
9. Loss of hair (hare) *Go wa ga moriri*				
10. Other skin problems (ander) *Mathata a mangwe a letlalo*				

If yes, when did the skin problems start? Mark one answer.
Fa karabo ya gago ele ee, bothata jwa letlalo bo simolotse leng? Ka kopo, tshwaya karabo e le ngwe.

Questions:	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
During the last week/*Beke ee fetileng*										
During the last month/*Kgwedi ee fetileng*										
1-6 months ago/*Kgwedi ele ngwe go tse thataro 1-6*										
More than 6 months ago/*Go feta dikgwedi dile 6 tse di fetileng*										

- Do you use any skincare products and what type of products and when?________________________
  ____

Notes:____

INTERPRETATION (PRESENCE OF SKIN DISEASES): Total of all ÷ 10 =			
1: None – no medical attention needed	2: Trivial - not justify for medical attention	3: Moderate – justify medical attention	4: Severe sign – need early medical attention

Annexure B: Nordic occupational skin questionnaire – short version

NOSQ-2002/SHORT translation master – Nordic Occupational Skin Questionnaire

Instructions to the respondents are written in Italics.

Respondent ID: ____________

G1. Workplace: ______________________________

Department: ______________________________

G2. Are you

a man ☐ 1

a woman ☐ 2

G3. Year of birth: 19___

G5. What is your present occupation? ____________________________

Since when? _____ *(year)*

G6. What is your major activity at work? ____________________________

Since when? _____ *(year)*

G8. **Do you perform any other paid work regularly?**
G7. **How many hours per week do you work in your main job (on average)?** _____ *(hours/week)*

no ☐ 1

yes ☐ 2 **What kind of work?** ___________________________________

How many hours per week (on average)? ______ (*hours/week)*

D1. **Have you ever had <u>hand eczema</u>?**

no ☐ 1

yes ☐ 2

D2. **Have you ever had <u>eczema on your wrists or forearms</u> (excluding fronts of elbows)?**

no ☐ 1 *(if you also answered* "no" *to question D1 move to question A1)*

yes ☐ 2

D5. **When did you last have eczema on your hands, wrists or forearms?**
(one answer in each column if applicable)

	Hand eczema	Wrist/Forearm eczema
I have it just now	☐ 3	☐ 3
not just now but within the past 3 months	☐ 4	☐ 4
between 3-12 months ago	☐ 5	☐ 5
more than 12 months ago	☐ 6	☐ 6
In which year was the last time? *(make your best estimate)*	_____ *(year)*	_____ *(year)*

F1. Have you noticed that contact with certain materials, chemicals or anything else <u>in your work</u> makes your eczema worse? *(one answer in each column if applicable)*

	Hand eczema	Wrist/Forearm eczema
no	☐ 1	☐ 1
yes	☐ 2	☐ 2
What?	______________________	______________________
	______________________	______________________
don't know	☐ 0	☐ 0

F2. Have you noticed that contact with certain materials, chemicals or anything else <u>outside your work</u> makes your eczema worse? *(one answer in each column if applicable)*

	Hand eczema	Wrist/Forearm eczema
no	☐ 1	☐ 1
yes	☐ 2	☐ 2
What?	______________________	______________________
	______________________	______________________
don't know	☐ 0	☐ 0

F4. Does your eczema improve when you are away from your normal work (for example weekends or longer periods)? *(one answer in each column if applicable)*

	Hand eczema	Wrist/Forearm eczema
no	☐ 1	☐ 1
yes, sometimes	☐ 2	☐ 2
yes, usually	☐ 3	☐ 3
don't know	☐ 0	☐ 0

A1. Have you ever had an itchy rash that has been coming and going for at least 6 months, and at some time has affected skin creases? *(by skin creases we mean folds of elbows, behind the knees, fronts of ankles, under buttocks, around the neck, ears, or eyes)*

no	☐	1
yes	☐	2
don't know	☐	0