Short-term effects of selected barrier creams on skin barrier function

A. Vermaak

21696934

BSc Hons. (Physiology)

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

Supervisor: Mr. C.J. Van der Merwe

Co-supervisor: Prof. F.C. Eloff

November 2014

Preface

This mini-dissertation is submitted in partial fulfilment of the requirements for the degree *Magister Scientiae* in Occupational Hygiene at the Potchefstroom Campus of the North-West University. It was decided to use the article format for the purpose of the mini-dissertation. References are presented according to the guidelines of an accredited journal, namely *Annals of Occupational Hygiene*.

Chapter one is a general introduction on barrier creams and related factors, a problem statement, objectives and hypotheses. Chapter 2 is a literature study regarding barrier creams, skin anatomy and different factors influencing skin barrier parameters. Chapter 3 is an article with a brief introduction, method, statistical analysis and discussion. Chapter 4 is the concluding chapter with a summary, recommendations and limitations of the study.

Authors Contribution

The contribution of each of the authors is presented in Table 1.

Table 1: Authors contributions

Name	Contribution
Ms. A. Vermaak	• Planning and writing of literature study, statistical analysis and writing of the mini-dissertation. • Execution of the study.
Mr. C.J. Van der Merwe	• Assisted with the design of the study, statistical interpretation, reviewing the mini-dissertation.
Prof. F.C. Eloff	• Assisted with the planning, design of the study, statistical interpretation and review of the mini-dissertation.

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

I declare that I have approved this mini-dissertation and article and that my contribution as reflected in Table 1 is a true reflection of my actual contribution to the mini-dissertation.

Ms. A. Vermaak	Mr. C.J. Van der Merwe	Prof. F.C. Eloff

Acknowledgements

Firstly, I would like to thank my Heavenly Father for blessing me with abilities and for giving me the strength that was needed to complete the research.

I would like to thank the following people for their contribution and continued support that enabled me to complete the mini-dissertation.

- Mr. C.J. Van der Merwe, my supervisor, for his encouragement, support, constant involvement, and interest in my study.
- Prof. F.C. Eloff for his mentorship, motivation, vast knowledge and consistent help throughout the study.
- My friends for their love and support throughout the entire study:
  - Ms. H. Liversage
  - Ms. A. De Jong
  - Ms. A. Rautenbach
  - Ms. S. Botha
- Ms. L. Viljoen for her constant involvement, motivation and encouragement throughout the entire study.
- Mr. K. Scheepers for his knowledge and assistance with the interpretation and statistical analysis of the data.
- My classmates of 2013 for their motivation, encouragement, assistance and constant involvement throughout the entire study:
  - Ms. S. Jansen Van Rensburg
  - Mr. M. Meintjes
  - Mr. R. Nortje
  - Mr. J. Viljoen
- The honours group of 2013 for their assistance in gathering the raw data that was needed for this study.
- Prof L.A. Greyvenstein for the English language editing.

"*This mini-dissertation is dedicated to Jaap Vermaak*"

Table of contents **Page**

Preface i
Authors Contributions ii
Acknowledgements iii
Table of contents iv
List of tables viii
List of figures viii
List of symbols ix
List of abbreviations ix
Summary x
Opsomming xii

Chapter 1: General introduction 1

1.1 Overview 2
1.2 Problem statement 4
1.3 Parameters of barrier function 4
1.4 Objectives 5
1.5 Hypotheses 5
1.6 References 6

Chapter 2: Literature study 9

2.1 Introduction 10
2.2 General overview on barrier creams 10
2.3 Mechanism of action of barrier creams 11
2.4 Types of barrier creams 11
2.5 Controversy regarding barrier creams 12
2.6 Dermal absorption of diesel exhaust particulates (DEP) 13
2.7 Dermal absorption of nanoparticles 13
2.8 Anatomy and organisation of the skin 13
2.8.1 Skin barrier function 14

Table of Contents **Page**

2.8.2 Stratum corneum 14
2.8.3 Epidermal layer 15
2.8.4 Dermis and hypodermis 16
2.9 Skin surface parameters 16
2.9.1 TEWL (Transepidermal water loss) 17
2.9.2 Skin hydration 18
2.9.3 Skin surface pH 20
2.10 Skin thickness 21
2.11 Factors influencing skin surface parameters 22
2.11.1 Endogenous factors 22
2.11.1.1 Age 22
2.11.1.2 Gender 23
2.11.1.3 Anatomical site 23
2.11.1.4 Race 24
2.11.1.5 Dominant versus non-dominant forearm 25
2.11.2 Exogenous factors 26
2.11.2.1 Circadian rhythms 26
2.11.2.2 Seasonal changes 27
2.11.2.3 Relative humidity 27
2.11.2.4 Ambient air temperature 28
2.11.2.5 Skin cleansing 28
2.11.2.6 Smoking 29
2.11.2.7 Caffeine intake 29
2.12 Conclusion 30
2.13 References 31

Chapter 3 Article 37

3.1 Authors instructions 38
3.2 Abstract 40

Table of contents **Page**

3.3 Introduction 43
3.4 Method 45
3.4.1 Instrumentation 45
3.4.2 Barrier creams 46
3.4.3 Participants 46
3.4.4 Calibration 47
3.4.5 Acclimatisation 47
3.4.6 Anatomical sites 47
3.4.7 Application procedure of barrier creams 48
3.4.8 Ethical aspects 49
3.5 Statistical Analysis 49
3.6 Results 50
3.6.1 Total skin thickness 55
3.7 Discussion 55
3.7.1 Short-term effect of barrier creams on skin surface parameters 55
3.7.2 Differences between the two barrier creams 56
3.7.3 Differences between the two racial groups 57
3.7.4. Total skin thickness 58
3.8 Conclusion 59
3.9 References 60

Chapter 4 Concluding Chapter 62

4.1 Summary 63
4.2 Recommendations 66
4.2.1 Recommendations for future laboratory studies 66
4.2.2 Recommendations for the use of barrier creams 66
4.3 Limitations 66
4.3.1 General challenges with barrier creams 67
4.3.2 Barrier creams: The working environment 67
4.4 References 69

Table of contents **Page**

Chapter 5 Appendix 70

5.1 Appendix 71
5.1.1 Table 71
5.1.2 Informed consent form 71

List of tables **Page**

Table 1: Authors Contributions ii

Chapter 1

Table 2: Description of the two barrier creams that will be used in this research study 3

Chapter 2

Table 3: Range of TEWL values and the interpretation thereof 18
Table 4: Range of skin hydration values and the interpretation thereof 19
Table 5: Range of skin surface pH and the interpretation thereof 21

Chapter 3

Table 1: Categories indicating positive or negative effect elicited by a barrier cream 59
Table 2: Effects of barrier creams on skin surface parameters used in this research study 59

Chapter 5

Table 3: Indicates *p*-values for different groups at different time intervals 72
Table 4: Indicates mean- and *p*-values for total skin thickness (for the mid-forearm and palm of the hand). 73

List of figures

Figure 1: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for TEWL for both anatomical sites (mid-forearm and palm) 51
Figure 2: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for skin hydration for both anatomical sites (mid-forearm and palm) 52
Figure 3: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for skin surface pH for both anatomical sites (mid-forearm and palm). 54

List of symbols

µl	Microlitres
°C	Degrees Celsius
%	Percentage
ml	Millilitres
cm	Centimetres
mm	Millimetres
nm	Nanometres
>	Greater than
<	Smaller than
g m^{-2} h^{-1}	Water vapour flux density

List of abbreviations

DEP	Diesel Exhaust Particulates
FA	Formaldehyde
HA	Hyaluronic Acid
IL	Interleukin
MPA	Multi Probe Adapter
NMF	Natural Moisturising Factor
pH	Potential of Hydrogen Ions
PPE	Personal Protective Equipment
RH	Relative Humidity
SAIOH	Southern African Institute for Occupational Hygiene
TEWL	Transepidermal Water Loss

Summary

Background: Barrier creams are applied to the surface of the skin to form a barrier that aims to prevent the penetration of irritants and allergens through the skin surface. Several inconsistencies and controversies exist in literature regarding the effect that barrier creams may have on skin barrier function. Various skin surface parameters are used to evaluate the effect that the barrier creams have on skin barrier function. These parameters include transepidermal water loss (TEWL), skin hydration and skin surface pH. Total skin thickness may be assessed as a variable on its own. Differences may exist in skin surface parameters when comparing African participants with Caucasian participants.

Aim: The specific aim of this research was to evaluate the short-term[1] effects of selected barrier creams on skin barrier function.

Note 1: The words short-term are used in this study as each barrier cream is only tested over a period of 8 hours and not tested over a long term period of months or years.

Method: Forty two non-smoking participants were included and tested in this study, of which 21 were African and the rest Caucasian. TEWL, skin hydration and skin surface pH were used to evaluate the differences in the effect of two different barrier creams (Reinol Solvgard and Momar Chex) on skin barrier function. TEWL was measured by making use of a closed chamber Vapometer (Deflin Technology Ltd., Kuopio, Finland), skin hydration using a Corneometer® CM 825 and skin surface pH using a pH meter probe (Courage and Khazaka Electronic Köln, Germany). A micro-pipette was used to drip a standard volume of 20 µl of ultrapure water on the skin surface before the researcher placed the pH meter probe onto the skin surface. Total skin thickness was measured by making use of ultrasound (Ultrascan 22 - TBS0061B) (Courage and Khazaka Electronic Köln, Germany). Three consecutive measurements were taken on the mid-forearm and the palm of the experimental arm. After baseline values were measured, 5 ml of the selected barrier cream was applied to the experimental arm. The barrier cream (selected for the day) was reapplied after 2, 4 and 6 hours and measurements were taken every 2, 4, 6 and 8 hours. The total skin thickness was measured at time zero and at 8 hours.

Results:

*TEWL***:** For both barrier creams, statistical significant differences ($p \leq 0.05$) were found between TEWL on the palms of African participants and Caucasian participants.

Skin hydration: Statistically significant differences ($p \leq 0.05$) were obtained with regard to mid-forearm skin hydration when comparing Reinol Solvgard with Momar Chex (this was applicable to both racial groups). A statistically significant difference ($p \leq 0.05$) was obtained with regard to mid-forearm skin hydration when comparing African participants with Caucasian participants (this was only applicable to Reinol Solvgard). Statistical significant differences ($p \leq 0.05$) were obtained with regard to skin hydration palm when comparing Reinol Solvgard with Momar Chex (this was applicable to both racial groups). Statistically significant differences ($p \leq 0.05$) were obtained with regards to skin hydration palm when comparing African participants with Caucasian participants (this was applicable to both barrier creams).

Skin surface pH: A statistically significant difference ($p \leq 0.05$) was obtained with regard to pH of the mid-forearm when comparing Reinol Solvgard with Momar Chex (this was applicable to only the African participants). A statistical significance ($p \leq 0.05$) was obtained with regards to skin surface pH mid-forearm when comparing African participants with Caucasian participants (this was applicable to Momar Chex barrier cream only). A statistically significant difference ($p \leq 0.05$) was obtained with regards to the pH of the palm when comparing Reinol Solvgard with Momar Chex (this was only applicable to the African racial group).

Conclusion: Using skin surface parameters, it can be concluded that Momar Chex barrier cream elicited more positive effects on skin barrier function than Reinol Solvgard barrier cream. This may be ascribed to the fact that both barrier creams lowered TEWL (positive effect), Reinol Solvgard lowered skin hydration (negative effect) whereas, Momar Chex increased the skin hydration (positive effect) and both barrier creams increased skin surface pH (negative effect). Furthermore, the objectives of this study were reached as (a) short-term effects on skin surface parameters were identified between African versus Caucasian participants, (b) significances were observed between the two barrier creams (Momar Chex and Reinol Solvgard) by making use of skin surface parameters and (c) general increases and or decreases were observed in skin surface parameters over a short term period of 8 hours.

Keywords: transepidermal water loss, skin hydration, skin surface pH, Reinol Solvgard barrier cream, Momar Chex barrier cream, African racial group, Caucasian racial group, skin barrier function.

Opsomming

Agtergrond: Beskermingsrome word aangewend op die veloppervlakte om ‘n beskermingslaag te vorm wat verhoed dat irritante en allergene deur die vel penetreer. Daar is talle tekortkominge en teenstrydighede in die literatuur, veral ten opsigte van die effek wat beskermingsrome op die velgrensfunksie het. Verskeie veloppervlak parameters word gebruik om die effek wat beskermingsrome op die velgrensfunksie het, te evalueer. Dit sluit die volgende in: trans-epidermale water verlies (TEWV), velhidrasie en die pH van die vel. Totale veldikte word geasesseer en geëvalueer as ‘n veranderlike op sy eie. Verskille kan voorkom in veloppervlak parameters wanneer Afrikaan proefpersone vergelyk word met Kaukasiese proefpersone.

Doelstelling: Die spesifieke doelstelling van hierdie navorsing was om die kort-termyn[2] effekte wat geselekteerde beskermingsrome op die velgrensfunksie het, te evalueer.

Nota 2: Die woorde kort-termyn word gebruik in hierdie studie omdat die beskermingsrome slegs oor ’n periode van 8 ure gemeet was en nie oor ’n lang termyn periode van maande of jare nie.

Metode: Twee en veertig proepfersone was ingesluit as deel van hierdie studie, waarvan 21 Afrikane was en die res Kaukasiërs. TEWV, vel-hidrasie en vel-oppervlak pH is gebruik om die verskille in die effekte van twee verskillende velbeskermingsrome (Reinol Solvgard en Momar Chex) op die velbeskermingsfunksie het, te evalueer. TEWV is gemeet met ’n geslote-kamer Vapometer (Deflin Technology Ltd., Kuopio, Finland), vel-hidrasie met ‘n Corneometer ® CM 825 en vel-oppervlak pH met ’n pH-meter-sensor (Courage and Khazaka Electronic Köln, Germany). ’n Mikro-pipet is gebruik om ‘n standaard volume van 20 µl “ultrapure” water op die vel te drup voordat die navorser die pH-meter-sensor op die vel-oppervlak geplaas het. Totale veldikte is gemeet deur gebruik van ultrasoniese klankgolwe (Ultrascan 22 - TBS0061B) (Courage and Khazaka Electronic Köln, Germany). Drie opeenvolgende meetings is geneem op die mid-voorarm en palm van die eksperimentele arm. Nadat die basislyn-waardes gemeet is, is ’n standaard volume van 5 ml velbeskermingsroom op die vel-oppervlakte van die eksperimentele arm aangewend. Die velbeskermingsroom (soos geselekteer vir daardie dag) is her-aangewend elke 2, 4 en 6 ure en metings is geneem elke 2, 4, 6 en 8 ure. Dit moet noteer word dat totale vel-dikte gemeet is by tyd 0 en weer na 8 ure.

Resultate: *TEWV:* Vir beide beskermingsrome is statisties betekenisvolle verskille ($p \leq 0.05$) gevind tussen die TEWV op die palm van Afrikaan-proefpersone en die Kaukasiese proefpersone.

Velhidrasie: Vir beide rassegroepe is statistiese betekenisvolle verskille ($p \leq 0.05$) gevind tussen Reinol Solvgard en Momar Chex met betrekking tot vel-hidrasie op die mid-voorarm. ’n Statistiese betekenisvolle verskil ($p \leq 0.05$) is gevind tussen Afrikaan-proefpersone en Kaukasiese proefpersone met betrekking tot velhidrasie op die mid-voorarm. Dit was slegs van toepassing op Reinol Solvgard beskermingsroom. By beide rassegroepe is statistiese betekenisvolle verskille ($p \leq 0.05$) gevind tussen Reinol Solvgard beskermingsroom en Momar Chex beskermingsroom met betrekking tot velhidrasie op die palm. By beide beskermingsrome is statisties betekenisvolle verskille ($p \leq 0.05$) gevind tussen Afrikaan-proefpersone en Kaukasiese proefpersone met betrekking tot die velhidrasie van die palm.

Vel-oppervlak pH: By die Afrikaan-proefpersone is ’n statisties betekenisvolle verskil ($p \leq 0.05$) gevind tussen Reinol Solvgard beskermingsroom en Momar Chex beskermingsroom met betrekking tot vel-oppervlak pH op die mid-voorarm. Vir Momar Chex beskermingsroom is ’n statisties betekenisvolle verskil ($p \leq 0.05$) gevind tussen Afrikaan-proefpersone en Kaukasiese proefpersone met betrekking tot vel-oppervlak pH op die mid-voorarm. By die Afrikaan rasgroep het ’n statisties betekenisvolle verskil ($p \leq 0.05$) bestaan tussen Momar Chex beskermingsroom en Reinol Solvgard beskermingsroom met betrekking tot vel-oppervlak pH op die palm.

Gevolgtrekking: Deur gebruik te maak van vel-oppervlak parameters, kan daar waargeneem word dat Momar Chex beskermingsroom meer positiewe effekte op die velbeskermingsfunksie het as Reinol Solvgard velbeskermingsroom. Hierdie redenering mag toegeken word aan die feit dat altwee beskermingsrome TEWV verlaag het (positiewe effek), Reinol Solvgard het die vel-hidrasie verlaag (negatiewe effek) waar, Momar Chex die vel-hidrasie verhoog het (positiewe effek) en beide beskermingsrome het die vel-oppervlak pH verhoog (negatiewe effek). Die doelstelling van hierdie studie was bereik omdat (a) die kort-termyn effekte op vel-oppervlak parameters opgemerk was tussen Afrikaan en Kaukasiese proefpersone, (b) statistiese betekenisvolle verskille gevind was tussen die twee beskermingsrome (Momar Chex en Reinol Solvgard) deur gebruik te maak van vel-oppervlak parameters en laastens (c) algemene verhogings en verlgaings was gevind in vel-oppervlak parameters oor ’n kort-termyn periode van 8ure.

Sleutel-woorde: transepidermale water verlies, velhidrasie, vel-oppervlak pH, Reinol Solvgard velbeskermingsroom, Momar Chex velbeskermingsroom, Afrikaan ras groep, Kaukasiese ras-groep, velbeskermingsfunksie.

CHAPTER 1: INTRODUCTION

General Introduction

1.1 Overview

The skin is the body's first line of defence against the external environment, protecting the body against the penetration of possible pathogens, allergens or chemicals and therefore, plays a crucial role in the regulation of internal homeostasis (Agache, 2004). The stratum corneum layer (uppermost layer of the skin surface) is an effective and primary barrier that provides protection against the above mentioned allergens or irritants. When the barrier is compromised through external factors it may lead to an increase in uptake of substances through the skin surface that may lead to local or even systemic toxic effects (Alvarez *et al*., 2001).

Different occupations expose the skin surface of workers to a variety of stressors including mechanical, chemical and physical stressors (Alvarez *et al*., 2001; Agner and Held, 2002). Occupations may include employees performing wet work, carpenters, machinists, health care providers and hairdressers amongst others (Agner and Held, 2002; Brown, 2004). According to a review article by Brown (2004), four million working days are estimated to be lost every year as a result of occupational diseases. Occupational contact dermatitis is one of the major occupational diseases that affect the hands of workers. Furthermore, hand dermatitis is a major concern as it arises more frequently with a duration period of more than 10 years (Agner and Held, 2002). Occupational skin diseases do not only play a detrimental role in the workplace by affecting the workers, but also affects the financial (economical) aspect of the business and therefore, various industries implement skin protection programmes to prevent occupational skin diseases. Skin protection programmes have several control measures that include reduction to exposure, technical control measures, personal protection, identification of susceptible individuals and education and training of workers (Agner and Held, 2002; Brown, 2004).

Barrier creams are only one of the personal protection measures used in the workplace to protect the worker against the possible penetration of skin irritants and allergens through the skin surface. Barrier creams are used to mimic the glove effect and to form a physical barrier (diffusion barrier) between the internal and external environment of the skin (Held *et al*.,1999; Berndt *et al*., 2000; Alvarez *et al*., 2001; Kresken and Klotz, 2003). Barrier creams are mostly applied to areas of the worker's skin surface that are exposed frequently and include the face, neck and hands (Held *et al*., 1999).

Barrier creams are used as a safety measure in several workplaces, yet major controversies arise with regards to the use and application of barrier creams between different racial groups. There are several prominent differences found in skin surface parameters between different racial groups, more specifically between African and Caucasian racial groups, these differences may be attributed to socioeconomic factors, geographical differences as well as nutritional and hygienic factors (Berardesca and Maibach, 2003; Diridollou *et al*., 2007). The differences between African skin and Caucasian skin still remains controversial as the thickness of the stratum corneum layer are equal between these races, but transepidermal water loss (TEWL) values are higher in African skin when compared to Caucasian skin. The measurement values obtained after measuring several skin surface parameters indicated that African subjects have a larger range of variance in data when compared to the data obtained from Caucasian subjects. Furthermore, African skin surface recover faster when compared to Caucasian skin surface when damaged (Berardesca and Maibach, 2003). The conflicting literature between the skin surface of different racial groups may indicate a potential differentiating effect that barrier creams may have on skin surface or barrier function in the African population when compared to the Caucasian population. Therefore, this factor needs to be investigated by using the same skin surface parameters to indicate if there are any possible differences between these two racial groups.

Type of barrier creams, ingredients and the use of barrier creams are of great interest when investigating barrier creams. Therefore, Table 2 illustrates the main differences in composition.

Table 2: Description of the two barrier creams that will be used in this research study.

Type of barrier cream	**Oil-Repellent (Water based)**	**Oil-Repellent (Water based)**
Product	Reinol Solvgard	Momar chex
Use	Protects against petrol, diesoline, paraffin and turpentine.	Protects against dirt, chemicals, liquids, grease and other materials that are difficult to remove.
Ingredients	• Waxes • Oils • Zinc oxide • Allantoin • Silicone free	• Emolients • Oils • Skin protective agents

1.2 Problem statement

The main controversy regarding the use of barrier creams in general is the effect that different barrier creams have on skin barrier function (Berndt *et al*., 2000; Alvarez, 2001). Some literature studies indicate that barrier creams protect the integrity of the stratum corneum by lowering TEWL, whereas other studies indicate an increase in TEWL creating controversy regarding the effectiveness of barrier creams (Held *et al*., 1999; Lodén *et al*., 1999; Alvarez *et al*., 2001; Madison, 2003; Du Plessis *et al*., 2013). In studies done by Held and Agner (2002) and Korinth *et al*. (2007) it was found that some barrier creams might even increase the permeability of chemicals or irritants through the skin surface. Scientific literature on the effect that barrier creams elicit on the skin barrier function is furthermore, very weak and differs between different barrier creams (Lodén *et al*., 1999; Larson, 2001; Nixon *et al*., 2006; Korinth *et al*., 2007; Korinth *et al*., 2008). These controversies will be addressed and discussed in detail in Chapter 2.

1.3 Parameters of barrier function

There are several parameters that are used to evaluate the integrity of the barrier function (Held *et al*., 1999; Lodén *et al*., 1999; Møller *et al*., 2003; Stefaniak *et al*., 2013). For this specific research the parameters used to evaluate the integrity of the barrier function will include TEWL, skin hydration and the apparent skin surface pH. These parameters will be used to evaluate the effect that the barrier creams have on barrier function.

TEWL measures the amount of water loss through the skin surface, skin hydration indicates the hydration state of the skin surface and the apparent skin surface pH is the concentration of hydrogen ions in the water solution of the stratum corneum that indicates the integrity of the skin surface (Agache, 2004; Rippke *et al*., 2004; Verdier-Sévrain and Bonté, 2007; Imhoff *et al*., 2009). These skin parameters will be discussed in detail in Chapter 2.

Total skin thickness is a variable that will be evaluated on its own, especially the effect that barrier creams or moisturisers have thereon. Studies on the effect that moisturisers have on skin thickness are controversial. Some studies indicate an increase in skin thickness while others, indicate a decrease. Skin thickness will be measured to assess or to evaluate the effect that barrier creams have on the total thickness of the skin (Crowther *et al*., 2008).

1.4 Objectives

It was the specific objectives of this study to compare:

- The short-term effects that selected barrier creams have on skin barrier function and skin thickness of African skin in comparison with Caucasian skin.
- Momar Chex barrier cream and Reinol Solvgard barrier cream with one another using identical skin parameters (TEWL, skin hydration, skin surface pH and total skin thickness).
- How different skin surface parameters are affected over a total time period of 8 hours for both barrier creams.

1.5 Hypotheses

Hypothesis 1

The application of barrier creams will have a general positive effect on the skin barrier function parameters over the short term (over a period of 8 hours). General positive effects may be categorised upon a barrier cream that lowers TEWL and skin surface pH and increases skin hydration.

Hypothesis 2

The difference in effect of two different brands of water based (oil repellent) barrier creams (Reinol Solvgard and Momar Chex) on skin barrier function will not be statistically significant (over a period of 8 hours).

Hypothesis 3

A statistical significant difference exists between the effect elicited from the application of barrier creams over the short term on African versus Caucasian skin.

1.6 References

Agache P. (2004) The human skin: An overview. *In* Agache P, Humbert P, *eds*. Measuring the skin. Springer. p. 3-28. ISBN 3 540 01771 2.

Alvarez MS, Brown LH, Brancaccio RR *et al*. (2001) Are barrier creams actually effective? Curr Allergy Asthma Reports; 1: 337-341.

Agner T, Held E. (2002) Skin protection programmes. Contact Dermatitis; 47: 253-256.

Berardesca E, Maibach H. (2003) Ethnic skin: Overview of structure and function. J Am Acad Dermatol; 48: 139-142.

Berndt U, Wigger-Alberti W, Gabard B *et al*. (2000) Efficacy of a barrier cream and its vehicle as protective measures against occupational irritant contact dermatitis. Contact Dermatitis; 42: 77-80.

Brown T. (2004) Strategies for prevention: occupational contact dermatitis. Occup Med; 54: 450-457.

Crowther JM, Sieg A, Blenkiron P *et al*. (2008) Measuring the effects of topical moisturisers on changes in stratum corneum thickness, water gradients and hydration *in vivo*. Br J Dermatol; 159: 567-577.

Diridollou S, De Rigal J, Querleux B *et al*. (2007) Comparative study of the hydration of the stratum corneum between four ethnic groups: influence of age. Int J Dermatol; 46: 11-14.

Du Plessis J, Stefaniak A, Eloff F *et al*. (2013) International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: Part 2. transepidermal water loss and skin hydration. Skin Res Technol; 19: 265-278.

Held E, Sveinsdóttir S, Agner T *et al*. (1999) Effect of long-term use of moisturiser on skin hydration, barrier function and susceptibility to irritants. Acta Derm Venereol; 79: 49-51.

Imhof RE, De Jesus MEP, Xiao P *et al*. (2009) Closed-chamber transepidermal water loss measurement: microclimate, calibration and performance. Int J Cos Sci; 31: 97-118.

Korinth G, Weiss T, Penkert S *et al*. (2007) Percutaneous absorption of aromatic amines in rubber industry workers: impact of impaired skin and skin barrier creams. Occup Environ Med; 64: 366-372.

Korinth G, Lüersen L, Schaller KH *et al*. (2008) Enhancement of percutaneous penetration of aniline and *o*-toluidine *in vitro* using barrier creams. Toxicology; 22: 812-818.

Kresken J, Klotz A. (2003) Occupational skin-protection products - a review. Int Arch Occup Environ Health; 76: 355-358.

Larson E. (2001) Hygiene of the skin: when is clean too clean? Emerg Infect Diseases; 7: 225-228.

Lodén M, Andersson AC, Lindberg M *et al*. (1999) Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (Canoderm®). Br J Dermatol; 140: 264-267.

Madison KC. (2003) Barrier function of the skin: “La Raison d’Être” of the epidermis. J Invest Dermatol; 121: 231-241.

Møller JS, Poulsen T, Wulf HC *et al*. (2003) Epidermal thickness at different body sites: Relationship to age, gender, pigmentation, blood content, skin type and smoking habits. Acta Derm Venereol; 83: 410-413.

Nixon R, Roberts H, Frowen K *et al*. (2006) Knowledge of skin hazards and the use of gloves by Australian hairdressing students and practicing hairdressers. Contact Dermatitis; 54: 112-116.

Rippke F, Schreiner V, Doering T *et al*. (2004). Stratum corneum pH in atopic dermatitis: Impact on skin barrier function and colonization with Staphylococcus aureus. Am J Clin Dermatol; 5: 217-223.

Stefaniak A, Du Plessis J, John S *et al*. (2013) International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: part 1. pH. Skin Res Technol; 19: 59-68.

Verdier-Sévrain S, Bonté F. (2007) Skin hydration: a review on its molecular mechanisms. J Cos Sci; 6: 75-82.

CHAPTER 2: LITERATURE STUDY

2.1 Introduction

The skin is one of the body's largest organs and it is the first line of defence against the external environment and contributes to several physiological functions in order to maintain a constant milieu. The skin surface, which forms the skin barrier, has several general functions for the sustainment of human life. These functions include, self-repair after damage was sustained, acting as a barrier against any mechanical or chemical stressors and finally protection against several pathogenic micro-organisms (Agache, 2004). Skin barrier function is one of the topics often investigated by researchers as there are several factors that may compromise the skin barrier. The effects that different barrier creams or moisturisers have on the skin barrier function are one of the areas of interest. Barrier creams are used in the industry or workplace and may be referred to as an invisible glove, however barrier creams do not replace gloves (Kresken and Klotz, 2003). In this chapter different occupations, barrier creams and several other factors concerning the skin will be discussed in detail. Furthermore, the skin anatomy and organisation will be discussed in depth. Several exogenous and endogenous factors influencing skin surface measurements will also be discussed.

2.2 General overview on barrier creams

Barrier creams or skin-protection creams are applied to the surface of the skin to form a physical barrier that provides protection against the penetration or absorption of any external stressors (Baur *et al*., 1998; Alvarez *et al*., 2001). The skin surface of workers is exposed to a variety of stressors that include mechanical, physical and chemical stressors. Other stressors that workers are exposed to include irritants and allergens that may lead to toxic or systemic effects (Alvarez *et al*., 2001). Several occupations where workers encounter stressors include employees performing wet work, carpenters, machinists, health care providers and hairdressers amongst others. Furthermore, these workers are exposed to several different irritants and a few of them include oils, solvents, wet work, acids and alkalis (Chew and Maibach, 2003). Occupational contact dermatitis is a disease commonly associated when workers hands, face or neck are exposed to irritants (Agner and Held, 2002). Occupational contact dermatitis has a major impact on the health of the workers as well as on the economical aspect of the business as several workdays are lost (Chew and Maibach, 2003). Skin protection programmes have been implemented in order to prevent skin diseases or to reduce the occurrence thereof (Agner and Held, 2002).

Barrier creams are applied to the skin surface of workers to prevent penetration or the absorption of several allergens or irritants through the skin surface (Alvarez *et al*., 2001).

2.3 Mechanism of action of barrier creams

Barrier creams are used in the work setting and it is of great importance that the mechanism of action is understood, especially when making use of biological monitoring to evaluate the efficacy of barrier creams (Drexler, 2003). There is controversy regarding the precise mechanism of action of barrier creams, yet research propose several mechanisms of action. In a study done by Drexler (2003) he states that skin protection creams can afford protection through three different ways 1) mechanical protection, 2) chemical protection or 3) that barrier creams can regenerate the barrier after it has been damaged. Alvarez *et al*. (2001) state that barrier creams are widely used as an effective barrier that defend the assault of external stressors, the precise mechanism remain unclear (Alvarez *et a*l., 2001). In contrast to Drexler (2003), Alvarez *et al*. (2001) stated that the mechanism of action of barrier creams may be due to any of the several ingredients in barrier creams. Ingredients may include tannery substances, zinc oxide and chelating agents. It is stated that zinc oxide has a shielding effect, whereas tannin hardens the skin's surface. The other proposed mechanism of action is that chelators bind with metal ions to prevent penetration thereof through the skin surface. Different mechanisms of action might explain the controversy regarding the effect that barrier creams have on the skin barrier function, especially detrimental effects (Alvarez *et al*., 2001). These detrimental effects may be due to the fact that some skin protection creams contain surfactant as an ingredient that paradoxally enhances the penetration of substances through the skin surface (Drexler, 2003).

2.4 Types of barrier creams

Several types of barrier creams exist and they may be categorised based upon the substances to which they afford protection (Alvarez *et al*., 2001). These may include water-repellent, oil-repellent and silicone repellent barrier creams. The most popular types of barrier creams used are the water and oil-repellent types of barrier creams. Water-repellent barrier creams protect the skin surface of workers against acids, alkalis, detergents, soaps and water-soluble solvents, whereas oil-repellent barrier creams protect the skin surface of workers against organic solvents, oils and varnishes (Alvarez *et al*., 2001).

2.5 Controversy regarding barrier creams

The main function of barrier creams is to prevent the penetration or absorption of chemicals, allergens or irritants through the skin surface of workers, yet the specific effect that barrier creams have on skin barrier function remains controversial (Berndt *et al*., 2000; Alvarez *et al*., 2001). As the composition of barrier creams differ, the difference in the ingredients may explain the diverse effect on the skin barrier function. In contrast, some barrier creams may contain fragrances, preservatives, emollients or emulsifiers that may lead to sensitisation in certain individuals susceptible to allergens and irritants (Alvarez *et al*., 2001).

Several studies indicate that barrier creams protect the integrity of the stratum corneum by lowering TEWL, whereas other studies indicate an increase in TEWL (Held *et al*., 1999; Lodén *et al*., 1999; Alvarez *et al*., 2001; Madison, 2003; Du Plessis *et al*., 2013). An increase in TEWL is an indication of damage to the barrier function, therefore, if barrier creams increase the TEWL it may be evident that the barrier cream has a negative effect on the barrier function (Alvarez *et al*., 2001).

In studies done by Held and Agner (2001) and Korinth *et al*. (2007) it was found that some barrier creams might even increase the permeability of chemicals or irritants through the skin surface acting as a transport vehicle. Scientific literature on the effect that barrier creams elicit on the skin barrier function is furthermore, very weak and differs between different types of barrier creams (Lodén *et al*., 1999; Larson, 2001; Nixon *et al*., 2006; Korinth *et al*., 2007; Korinth *et al*., 2008).

In some instances barrier creams are incorrectly referred to as moisturisers and *vice versa*. Barrier creams are used throughout the workday shift, more specifically every four hours, whereas moisturisers are used at the end of the work day shift to hydrate the surface of the skin (Kresken and Klotz, 2003).

Some studies recommend that barrier creams should be used in addition with protective gloves ensuring further protection, yet this is not necessarily the case. The ingredients of the barrier cream may act as a transmission vehicle for allergens or irritants. These stressors may originate from the powder of the gloves. Penetration of irritants and allergens through the skin surface (barrier function) may elicit an allergic reaction (Baur *et al*., 1998).

2.6 Dermal absorption of diesel exhaust particulates (DEP)

Oil-repellent barrier creams, for example Reinol Solvgard barrier cream, prevents the penetration of diesel exhaust particulates (DEP) through the surface of the skin. Only small amounts of exposure to DEP and Formaldehyde (FA), especially on the hands are necessary to change the cytokine levels. It has been found that keratinocytes lead to the production of Interleukin (IL) - 8 and it is controlled by the release of protein kinase C. An increase in dermal exposure to DEP or FA from an automobiles exhaust leads to an increase in levels of IL-8 and this increased level of IL-8 leads to a condition, namely hyperkeratosis, which is one of the symptoms of atopic dermatitis (Ushio *et al*., 1999).

2.7 Dermal absorption of nanoparticles

From studies it is evident that workers in future will be exposed to nanoparticles. Nanomaterials are defined as particles that have one dimension < 100 nm. Nanomaterials or particles can be divided into two general groups, one being particles that are not engineered and the other group that is engineered or either controlled. Nanoparticles are of importance for the fact that they are found in several sunscreens, barrier creams and in several cleaning products. Dermal absorption is of great concern as it is one of the routes of absorption. Zinc oxide is one of the ingredients that is found in some barrier creams and is classified as a nanaoparticle, yet authors found no zinc oxide in the lower part of the stratum corneum of the skin surface suggesting that there was no penetration of zinc oxide through the epidermis (Crosera *et al*., 2009).

The major concern with nanoparticles or nano products is the fact that due to their size they may penetrate the dermal layer of the skin surface and elicit harmful effects such as forming free radicals that may finally lead to DNA damage. It is evident that zinc oxide that is found in several barrier creams is not harmful, yet other nanoproducts may be harmful. Examples of nanoproucts include silver, gold nanoparticles found in textiles and contraceptives. Nanoparticles may be toxic to keratinocyte cells in the superficial layer of the skin surface (Crosera *et al*., 2009).

2.8 Anatomy and organisation of the skin

The skin is commonly referred to as the origin of the barrier function and has several layers that include the stratum corneum, epidermis and hypodermis.

Each of these layers has their own specific physiological functions (Agache, 2004). Skin barrier function and these separate layers will now be discussed.

2.8.1. Skin barrier function

The skin's crucial function is to act as a physical barrier between the inside (which includes the internal structures and organs of the organism) and the outside (which includes the immediate environment). The barrier protects the organism in this case the human body - against several physical and chemical stressors as well as against microbes that may cause harm should it penetrate the internal environment. Should the barrier function be compromised through any of the several work related allergens or irritants, occupational dermatitis may occur. As time progresses or exposure increases, irritant or allergic contact dermatitis may develop (Proksch and Brasch, 2011).

The skin barrier consists of three types of barriers that include a physical, chemical and immunological barrier. The immunological barrier is the adaptive type of barrier (Proksch and Brasch, 2011). The cells that form part of the immunological barrier include the Langerhans cells located in the epidermal layer of the skin surface, the endothelial cells and the keratinocyte cells (Bos, 1997). Although the stratum corneum is regarded as the main component of the physical barrier, the epidermis also forms part of the physical barrier. The chemical barrier contains various lipids, peptides, lysozymes and acids that protect the body against the penetration of chemicals. The immune barrier protects against several allergens that may lead to an allergic reaction (Proksch and Brasch, 2011).

As reference to the barrier function of the skin usually implies the physical barrier function of the skin, the stratum corneum and epidermal layer will now be discussed.

2.8.2 Stratum corneum

The most superficial layer of the skin, the stratum corneum layer, is an essential physical barrier that is approximately 20 µm thick which forms a barrier between the underlying tissue and the immediate environment (Tagami *et al*., 1980; Behne *et al*., 2003; Proksch and Brasch, 2011). Furthermore, this layer functions as a barrier that regulates flux (inward and outward movement) of different chemicals and water between the skin surface of the human and the external environment. In order to maintain homeostasis (flux) the stratum corneum's integrity should be in an impeccable state (Berthaud and Boncheva, 2011).

To assess the integrity of the stratum corneum, several skin surface parameters are used, and they include TEWL, the hydration state of the stratum corneum and the skin surface pH. Low skin surface pH and TEWL and high levels of skin surface hydration are signs of a stratum corneum being in an impeccable state (Berthaud and Boncheva, 2011). Therefore, these parameters are measured to indicate the integrity of the stratum corneum layer or skin barrier function. According to Proksch and Brasch (2011) these, different parameters may be influenced when topical products such as barrier creams or moisturisers are applied. Measurements of these parameters may indicate the effect that barrier creams have on the stratum corneum. These parameters will be individually discussed in this chapter.

2.8.3 Epidermal layer

The epidermal layer of the skin surface consists of keratinocyte cells which function it is to protect against the penetration of harmful irritants or allergens through the surface of the skin. Keratinocytes need to undergo constant differentiation and proliferation processes. Keratinocytes start out as corneocyte cells that are joined tightly through gap junctions. Furthermore, these corneocytes are covalently bound to the cell membranes proteins and these proteins are called corneodesmosomes. Corneocytes differentiate from the basal epidermal layer towards the stratum corneum's surface (outermost layer). This process is called the keratinisation of the epidermal layer. In the final stages of the keratinisation process there is a change in the keratinocytes structure leading to the flattened squamous cells of the stratum corneum. Corneocytes have keratin filaments which function is to protect against mechanical forces. Corneocytes are surrounded by nonpolar lipids which forms a hydrophobic layer. The proteins and lipids of the corneocytes are of importance as they protect against chemical factors, but also lead to water-impermeability through the skin surface. The proteins account 7 ─ 10% of the total mass of the epidermal layer (Proksch and Brasch, 2011).

Corneocytes need to maintain homeostasis; this is achieved through termination or cell loss after a specific amount of time. Termination or desquamation is made possible when cells are weakened and when they move outwards towards the skin surface. Desquamation of corneocytes is needed as these cells are constantly exposed to several mechanical, chemical and physical factors. In the deeper layers of the stratum corneum there is filaggrin and when it degrades it stimulates Natural Moisturising Factor (NMF) to hydrate the deeper layers (Agache, 2004; Berthaud and Boncheva, 2011).

There is a balance between the differentiation and proliferation processes. A normal balance between these two processes indicates an impeccable stratum corneum, whereas an inbalance may compromise the integrity of the stratum corneum (Proksch and Brasch, 2011).

2.8.4 Dermis and Hypodermis

The dermis and hypodermis are located underneath the epidermal layer and contain sweat glands. There are millions of sweat glands that are needed for thermoregulation. The body can produce up to 10 litres of sweat daily, yet only 5% of sweat glands are active at any given time. These glands are located over the entire human body, yet there are several areas where they are absent. The major area of importance, especially for thermoregulation includes the soles of the feet, the forehead, the cheek, axilla and the palms of the hands. The sweat gland has a tubular structure with two portions, a secretory portion and a ductular portion. The duct part of the sweat gland fuses with the basis part of the epidermal papillae and then opens with a rounded aperture onto the surface of the skin, which is visible. The secretory portion has a diameter of approximately 0.5 mm and originates deep in the dermis. The secretory portion of the duct contains clear and dark cells. The clear cells function is to secrete water, electrolytes and sweat, whereas the dark cells function is to secrete glycoproteins. Glycoproteins are the proteins found in sweat and the rest of their functions have been poorly understood (Kreyden and Scheidegger, 2004).

Sweat starts as a hypotonic solution which is clear and odourless that contains chloride and sodium and several others constituents (Kreyden and Scheidegger, 2004).

The anatomy of the dermis and hypodermis is of importance due to its relevance to sweat glands. Sweat glands produce sweat that affects several skin surface parameters. The effect that sweat has on skin surface parameters will be discussed later in this chapter.

2.9 Skin surface parameters

Several skin surface parameters are used to evaluate the integrity of the barrier function. These skin surface parameters include TEWL, skin hydration and skin surface pH. These parameters will be discussed individually.

2.9.1 TEWL (Transepidermal water loss)

The main function of the stratum corneum layer of the skin is to prevent water loss from the internal environment through the skin surface (outward movement) which excludes the normal sweat that can be formed. TEWL is one of the skin surface parameters that have been used for more than a half century to measure the amount of water loss through the skin surface. TEWL is also used to indicate the integrity of the skin barrier function (Kalia *et al*., 2000; Imhof *et al*., 2009). The SI unit used for TEWL is g $m^{-2}h^{-1}$; that represents grams of water per square metre of skin for every hour (Imhof *et al.*, 2009). TEWL is defined as the insensible water loss through the surface of the skin (epidermis) through a process of evaporation and is measured by making use of several different types of instruments (Eberlein-König *et al*., 2000; Levin and Maibach, 2005; Farahmand *et al*., 2009; Imhof *et al*., 2009). There are two methods to measure TEWL, one method based on an open chamber principle and the other on a closed chamber principle. The closed chamber method provides a more stable environment for measurement of TEWL values as it is isolated from the outside environment when compared to that of the open chamber. This is an important concept of understanding as TEWL values differ between these two methods and accuracy is of great importance for any research. Therefore, the same method needs to be followed in any experiment (Imhof *et al*., 2009). The instrument measures TEWL by making use of a principle that measures the water gradient of the skin surface compared to the ambient air.

TEWL is a parameter that is used to indicate the physical integrity of the stratum corneum layer of the skin surface or barrier function, yet there are several factors influencing this parameter and include the anatomical site, sweating, temperature of the skin's surface, variation between different individuals, ambient temperature, relative humidity and variation between instruments (Eberlein-König *et al*., 2000; Levin and Maibach, 2005). These factors will be discussed in detail later in this chapter.

An increase in TEWL indicates an impairment of the water barrier function of the skin. Furthermore, TEWL is used to evaluate the effect of barrier creams on the barrier function as an increase in TEWL correlates with an increase in percutaneous absorption (Levin and Maibach, 2005; Farahmand *et al*., 2009). Percutaneous absorption can be defined as the rate of absorption of topically applied products through the skin surface. Some of the barrier creams used in the industry contain ingredients, for instance zinc oxide that are nanoparticles that are easily absorbed through the skin surface (Levin and Maibach, 2005). Therefore, an increase in TEWL found when barrier creams are measured may indicate an increase in percutaneous absorption that may be a disadvantage of barrier creams.

This above statement may be ascribed to the fact that both an increase in TEWL and percutaneous absorption are sings of an impaired water barrier (Levin and Maibach, 2005). An increase in TEWL can also be an indication of a dry skin surface (Eberlein-König *et al*., 2000).

Table 3: Range of TEWL values and the interpretation thereof (Deflin, 2010)

TEWL index ($gm^{-2}h^{-1}$	**Interpretation**
0 – 8	Very healthy skin barrier condition
8 – 14	Healthy skin barrier condition
14 – 20	Normal skin barrier condition
20 – 24	Strained skin barrier condition
> 25	Critical skin barrier condition (possible damage)

2.9.2 Skin hydration

Skin hydration is one of the skin surface parameters that can be measured to indicate the state the barrier is in. The stratum corneum layer of the skin surface plays an important role as it prevents water loss from the skin surface to the environment. Corneocyte cells have NMF that plays a role in the intercellular lipids. The dermal layer of the skin surface contains hyaluronic acid (HA), which is of hydrophilic nature which is also necessary for the hydration state of the stratum corneum (Verdier-Sévrain and Bonté, 2007). The specific role of the corneocytes is that they form the physical part of the stratum corneum layer and when cells are hydrated they contribute to several physiological functions. These cells contain keratin filaments and other molecules (including NMF) that are formed when they are broken down by filaggrin (Verdier-Sévrain and Bonté, 2007; Darlenski *et al*., 2009). Proteins surround the corneocytes that provide the mechanical resilience of the stratum corneum layer. The stratum corneum layer consists of 20% water, a part of which is bound to the lipids. The water content of the stratum corneum is influenced by the relative humidity (Verdier-Sévrain and Bonté, 2007).

The regulation of a healthy stratum corneum depends on two components from the differentiation process of the keratinocytes, one is the corneocytes and their NMF content and the other one is the intercellular lipids. Normal functioning of corneocytes (including their

NMF) and intercellular lipids will ensure an optimal state of hydration. The importance of a hydrated stratum corneum (high water content) is that the water plays a major role in several enzymatic processes that are needed for desquamation of corneocytes. When there is a decrease in the amount of water it affects the enzymatic function which relies on water for the desquamation process (Verdier-Sévrain and Bonté, 2007).

A decrease results in the desquamation process being impaired which leads to the formation or adhesion of corneocytes to the surface of the skin. This disadvantage leads to several physical symptoms which include flaking, dryness, scaling and roughness of the skin surface (Verdier-Sévrain and Bonté, 2007).

Low humidity, wind and exposure to the sun may lead to a decrease in the water content of the stratum corneum as these environmental conditions may affect the desquamation process and ultimately lead to dry and or flaky skin (Verdier-Sévrain and Bonté, 2007). In contrast to the physical characteristics of a dehydrated stratum corneum, a hydrated stratum corneum can be identified by physical characteristics that include a soft and flexible skin surface, and a general healthy appearance (Alanen *et al*., 2004).

High skin hydration values correlate with low TEWL values and *vice versa* (Darlenski *et al*., 2009). High water content can relate to good hydration of the stratum corneum, whereas low water content indicates dehydration of the stratum coneum (Tagami *et al*., 1980; Darlenski *et al*., 2009). Moisturisers are used to hydrate the stratum corneum layer of the skin surface (Verdier-Sévrain and Bonté, 2007).

Table 4: Range of the skin hydration values and interpretation thereof (Courage and Khazaka, 2008)

Hydration index	**Skin condition**
< 30	Very dry skin
35 – 45	Dry skin
>45	Sufficiently moisturised skin condition

2.9.3 Skin surface pH

The stratum corneum layer is known to have an acidic pH that ranges from 4 to 6. This acidic environment protects against several pathogenic organisms, plays a role in desquamation of the stratum corneum and assists with barrier homeostasis (Rippke *et al*., 2004; Schmid-Wendtner and Korting, 2006). Schmid-Wendtner and Korting (2006) state that the acidic stratum corneum has a sharp gradient that controls the activity of several enzymes and plays a role in the renewal of the skin surface.

The pH of the stratum corneum is based on a principle of the negative logarithm of the concentration of hydrogen ions in the watery solution of the stratum corneum. pH has a neutral point which is 7 and values that range from 0 (acidic) to 14 (alkaline). It is known that the skin surface pH is as a result of secretions from the sweat and sebaceous glands. Several studies made use of a flat planar glass electrode in order to measure the skin surface pH with water used as a contact medium between the glass electrode and the skin (Waller and Maibach, 2005; Schmid-Wendtner and Korting, 2006). Measurement of the pH of the skin surface needs to be referred to as apparent pH and this is due to the fact that the hydrogen ions which are measured, originate from the extracted material of the stratum corneum layer (Waller and Maibach, 2005).

The acidic pH of the stratum conreum is maintained through several products that are formed during exocrine secretion. These products include fatty acids from sebum, lactic acid from sweat and by-products that are formed through the keratinisation process (Rippke *et al*., 2004).

There are several proposed mechanisms that describe the origin of the acidic skin surface pH and two mechanisms of action have been proposed, one being an active mechanism and the other being of a passive nature. The passive mechanism requires no energy and produces lactic acid that is contained in eccrine sweat. Lactic acid then diffuses back through the surface of the skin and acidifies the stratum corneum. The active mechanism requires energy for the proton pumps to function. Both of these processes are likely to play a role and may be responsible for the acidification of the superficial layer of the skin surface (Lambers *et al*., 2006). There are several different factors affecting the skin surface pH and these factors will be described later in this chapter.

Table 5: Range of the skin surface pH values and interpretation thereof (Courage and Khazaka, 2008).

pH-Value on skin surface	<3.5	3.8	4.0	4.3	4.5	5.0	5.3	5.5	5.7	5.9	6.2	6.5	>6.5
Women	+ acidic range -				Normal				- High skin pH value +				
Men	+ acidic range -				Normal				- High skin pH value +				

2.10 Skin thickness

Skin thickness is measured by making use of ultrasound wavelengths to determine the total thickness of the skin. There are several controversial studies regarding the specific measurement of skin thickness. This controversy exists as several sections of the skin can be measured and they include the total skin thickness, the stratum corneum thickness or the epidermal skin thickness. These different sections differ in thickness (Waller and Maibach, 2005). Waller and Maibach (2005) indicated that there is a statistical significant difference in the stratum conreum thickness between different individuals. Waller and Maibach (2005) furthermore, stated that it is difficult to interpret the values obtained when measuring the epidermal skin thickness and total skin thickness. The major factors influencing the thickness of skin is exposure to the sun, elasticity properties and hormonal differences (Waller and Maibach, 2005).

There are certain symptoms of dermatological disorders that include dryness, flaking and scaling of the skin surface. This dry cycle that exists leads to epidermal hyperproliferation and defective differentiation that in the end leads to impaired skin barrier function and desquamatory properties. These disorders are commonly treated with moisturisers and the two parameters used to evaluate the effect include skin hydration and TEWL as mentioned previously. This is an important concept for the stratum corneum thickness as it is stated that some moisturisers may impair the skin barrier function by increasing the susceptibility for irritants through the skin surface, whereas other moisturisers are known to strengthen the skin barrier function. Furthermore, it is stated that short-term application of moisturisers has different effects on the stratum corneum thickness (Crowther *et al*., 2008).

Hydrophilic moisturisers reduce the stratum corneum thickness, yet 5% glycerol that is found in some barrier creams indicated a 25% increase in the stratum corneum thickness as there is a resultant swelling of corneocyte cells. As there is controversy with regards to the effect that different ingredients of moisturisers have on the stratum corneum thickness it indicates the need for further investigation. Furthermore, several studies referred to stratum corneum thickness, yet it may differ from total skin thickness (Crowther *et al*., 2008). Skin thickness is of importance as the rate of TEWL through the skin surface is directly proportional to the thickness (Treffel *et al*., 1994).

2.11 Factors influencing skin surface parameters

There are several factors that may influence skin surface parameters and these factors are divided into two main groups and include endogenous and exogenous factors. For precise and accurate values that can be interpreted these factors should be closely regulated or eliminated. These factors will be discussed in length.

2.11.1 Endogenous factors

Endogenous factors will now be discussed.

2.11.1.1 Age

Structural differences in the skin surface of infants and elderly people exist when compared to that the middle aged population groups. Skin surface pH values are higher in the young and elderly. Between the ages of 70 – 80 years there is an increase in the skin surface pH values (Waller and Maibach, 2005; Lambers *et al*., 2006, Stefaniak *et al*., 2013). This factor should be considered when groups with different mean ages are to be compared as skin surface pH values may differ due to age related changes. Parra and Paye (2003) state that the skin surface pH remains constant between the ages of 18 – 60 years. In order to compare different aged groups skin surface pH it is important that the same anatomical area is used and even if the same anatomical site is used cosmetic application may play a role in the skin surface pH (Schmid-Wendtner and Korting, 2006). An increase in age correlates with a decrease in stratum corneum hydration and finally leads to skin dryness (De Paepe *et al*., 2000). Skin thickness is seen as a variable on its own and skin thickness varies between different aged groups.

The epidermal layer of the skin surface is thinner in older individuals when compared to younger individuals this may be due to several morphological changes that are age related. The skin surface of older individuals is more susceptible to mechanical forces and gets easily damaged when compared to younger aged groups skin surface. There is a decreased proliferation in the epidermal layers of older individuals and this may influence the absorption rate when compared to younger aged individual's epidermal layer (Waller and Maibach, 2005). In an article by Du Plessis *et al*. (2013) he tabled that some studies indicated differences between age groups with regards to TEWL, whereas other studies did not indicate any differences.

2.11.1.2 Gender

There are contradictory values observed between male and female test subjects, especially with regards to skin surface pH. It is known that men have a more acidic skin surface pH when compared to female subjects; this may be due to the fact that female subjects are traditionally more prone to apply topically products than men (Lambers *et al*., 2006). Parra and Paye (2003) found no significant difference in the skin surface pH between men and women, yet they state that the minimal difference in skin surface pH may be due to cosmetic application. There are several studies that confirm that men have lower skin surface pH values when compared to women, yet other studies indicate an opposite effect and some studies even found no difference in the skin surface pH values between women and men (Lambers *et al*., 2006). Schmid-Wendtner and Korting (2006) stated that with several investigations they found men to have an average lower skin surface pH of 4.3 compared to women having a higher skin surface pH of 5.6. In a study done by Du Plessis *et al*. (2013) it was reported that there is no difference in skin hydration and TEWL between male and female participants.

2.11.1.3 Anatomical site

Normal skin surface pH values are noted at the normally assessed anatomical sites and includes the forearm, forehead, neck and cheek. Anatomical sites such as the axilla and intertriginous areas have higher skin surface pH values (Parra and Paye, 2003; Lambers *et al*., 2006). The anatomical site that is the most constant and frequently measured is the forearm (Lambers *et al*., 2006; Harmsze *et al*., 2008).

Treffel *et al*. (1994) state that different anatomical areas vary from one another in relation to skin hydration, TEWL and skin surface pH. Harmsze *et al*. (2008) state that when measuring the TEWL, the forearm should be used as the anatomical site. Although the palm of the hand is more prone to occlusion it should be measured as it is one of the anatomical sites most frequently exposed to irritants and allergens, especially in the working enviroment (Harmsze *et al*., 2008). Kleesz (2012) states that TEWL differs between different anatomical sites in both normal and in diseased skin.

Anatomical sites with the highest TEWL include the palms of the hands, the soles of the feet and the forehead. This tendency may be due to cofactors, which include occlusion and excessive sweating at these anatomical sites. Skin hydration between several different anatomical sites may vary and this may be due to stratum corneum thickness that differs between several different anatomical sites. This matter of interest needs further investigation as several controversial studies exist (Kleesz, 2012).

Skin thickness has been noted to vary between different anatomical sites due to the fact that there are different lipid fractions at different anatomical sites present. Anatomical sites that are exposed to the sun are known to be thicker than in comparison with areas less exposed to the sun (Fluhr *et al*., 2002).

2.11.1.4 Race

The simple difference between African subjects and Caucasian subjects is the pigmentation, where pigmented skin is different in their reaction to chemical and environmental factors and needs specific skin care (Fluhr *et a*l., 2008).

There are conflicting data available on the functional and structural differences between African skin when compared to Caucasian skin (Fluhr *et al*., 2008). Berardesca *et al*. (1998) stated that there is a difference in the stratum corneum, cell cohesion of the corneocyte cells and a difference in the desquamation process that is higher in African skin when compared to Caucasian skin. Fluhr *et al*. (2008) stated in a study that the stratum corneum thickness is equal between African and Caucasian skin, yet there is an increase in cell layers in African skin when compared to Caucasuan skin and the lipid content of the stratum corneum is higher in African skin when compared to Caucasian skin.

Fluhr *et al*. (2008) agrees with Berardesca *et al*. (1998) in the sense that the desquamatory process is higher in African skin when compared to Caucasian skin, and they continue and specify that this process is 2.5 times higher. Understanding possible structural and functional differences between these two racial groups is important as there are differences in several skin surface parameters. These differences in skin surface parameters between African and Caucasian skin will be discussed in detail. TEWL is higher in African subjects when compared to Caucasian subjects, yet penetration of external factors is lower (Treffel *et al*., 1994; Berardesca *et al*., 1998; Fluhr *et al*., 2008). Normally there is a correlation between TEWL and stratum corneum hydration, but this is not necessarily the same situation when comparing African skin with Caucasian skin (Fluhr *et al*., 2008). Fluhr *et al*. (2008) stated that most of the studies indicated no differences in stratum corneum hydration in African skin when compared to Caucasian skin, yet Treffel *et al*. (1994) indicated a difference in stratum corneum hydration between these two racial groups. There are conflicting studies available regarding the difference in the skin surface pH between different racial groups. Some studies indicate that Africans have a lower skin surface pH when compared to Caucasian skin surface pH, yet other studies indicate an opposite effect (Parra and Paye, 2003; Lambers *et al*., 2006; Schmid-Wendtner and Korting, 2006; Fluhr *et al*., 2008). The precise difference between these racial groups is not clear or specific, yet several possible explanations have been proposed.

2.11.1.5 Dominant versus non-dominant forearm

Treffel *et al*. (1994) found a statistical significant difference between the dominant and non-dominant forearm with regards to TEWL. Increased TEWL was measured on the dominant forearm when compared to the non-dominant forearm and this may be due to the fact that there is greater usage of the dominant arm than compared to the non-dominant forearm. The dominant arm is used in everyday activities such as writing that may lead to the disturbance of the stratum corneum causing increased water loss through the skin surface. The dominant forearm has a larger muscle as it is used more frequently and this leads to increased metabolism that may contribute to the increased TEWL when compared to the non-dominant forearm. Controversial studies exist on this subject as there are studies that found no statistical significant difference in TEWL values between the dominant and non-dominant forearm (Treffel *et al*., 1994). As there may be a difference between the dominant and non-dominant forearm there is a need for randomisation of the forearms when measurements are taken, especially in experimental studies (Treffel *et al*., 1994).

Kleesz (2012) stated that there was no significant difference between the left and right forearm, yet the TEWL was higher on the right arm when compared to the left forearm. The controversy regarding this statement is the fact that it was not indicated which arm is the dominant and non-dominant arm and this becomes a factor in several different studies that were conducted on the same topic. Skin hydration showed no significant difference between the left and right arm, yet higher values were measured on the left arm. In comparison with the previous statement higher skin surface pH values were found on the right arm (Kleesz, 2012).

An increase in TEWL correlates with increased skin surface pH. Increased TEWL on the dominant forearm as mentioned above then correlates with high skin surface pH on the dominant forearm than compared to the non-dominant forearm (Yosipovitch *et al*., 1998). Some studies indicate that there is a difference in skin surface pH, yet Parra and Paye (2003) states that there is no difference. In a recent study done by Stefaniak *et al*. (2013) he stated that data gathered between dominant versus non-dominant arms are conflicting with regards to skin surface pH.

2.11.2 Exogenous factors

Exogenous factors will now be discussed

2.11.2.1 Circadian rhythms

Circadian rhythm refers to the changes throughout the entire day and this relates specifically to skin surface parameters.

Differences were indicated in the skin surface pH values throughout the day. High skin surface pH values have been noted in the afternoon in comparison with low skin surface pH values measured at night (Lambers *et al*., 2006). Circadian rhythms have been linked to eccrine sweating as there are temperature changes throughout the day that may initiate or activate sweat secretion. Sweat secretion influences several skin surface parameters and will also be described as one of the exogenous factors (Yosipocitch *et al*., 1998). Parra and Paye (2003) found that circadian rhythms influence the skin surface pH at certain anatomical sites.

In the study done by Yosipovitch *et al.* (1998), circadian changes were noted in TEWL and skin surface pH. TEWL was lower in the mornings when compared to the afternoon and this may be due to the fact that skin temperature was higher in the afternoons when compared to the mornings. Yosipovitch *et al.* (1998) furthermore, found no correlation between circadian rhythms and skin surface hydration. Therefore, only TEWL and skin surface pH may be influenced by circadian rhythms.

2.11.2.2 Seasonal changes

The skin surface pH values are higher in the winter when compared to that of summer (Lambers *et al*., 2006). Parra and Paye (2003) indicates that there is a difference in the skin surface pH during different seasons and this is linked to the variation in temperatures between different seasons that lead to either an increase or decrease in sweat production. Rogers *et al.* (1996) found no correlation between the seasonal changes and the TEWL and this may be due to the fact that the changes of lipids between seasons are due to intrinsic factors only. In a study done by Egawa and Tagami (2008) there was no significant difference between the effect that seasonal changes have on the water content of the stratum corneum. TEWL and skin hydration are not affected by seasonal changes, only skin surface pH is influenced by this factor.

2.11.2.3 Relative humidity

Relative humidity is one of the aspects of microclimate that may affect the TEWL measurements (Imhof *et al*., 2009). TEWL is a diffusion process that is passive and therefore, the rate of diffusion through the skin surface is dependent on the relative humidity. As the relative humidity increases the stratum corneum's water content increases, thus there is a change in the diffusion coefficient (Grice *et al*, 1976). In a study done by Grice *et al*. (1976) there was an increase in TEWL as the relative humidity increased. The increase in relative humidity leads to activation of sweat that increases not only the TEWL, but also influences the accuracy of the TEWL. Treffel *et al*. (1994) stated that TEWL and skin hydration are affected by the relative humidity. The relative humidity needs to be regulated between 40 – 60% for accurate measurements of TEWL, skin hydration and skin surface pH (Imhof *et al*., 2009). Skin hydration and TEWL is influenced by the relative humidity (Treffel *et al*., 1994). It is evident that barrier creams may lead to occlusion and therefore, all the possible factors influencing TEWL need to be eliminated or regulated as far as is practically possible.

2.11.2.4 Ambient air temperature

Ambient air temperature affects the human body, and when there is an increase in the ambient room temperature this may activate the stimulation of sweat gland activity. An increase in sweat gland activity leads to an increase in the TEWL through the skin surface and this process is called thermoregulation (Grice *et al*., 1976). Both high and low temperatures affect the stratum corneum and the stratum corneum loses its ability to retain water. An increase in the temperature leads to a decrease in the hydration state of the stratum corneum (Spencer *et al*., 1975). Temperature affects the skin surface by increasing the sweat gland activity. An increase in sweat gland activity increases the sweat excretion and less potassium and chloride ions are reabsorbed creating a less acidic pH and increases the skin surface pH values (Ehlers *et al*., 2001).

There is an increase of 0.023 pH with every 1 °C increase in temperature (Parra and Paye, 2003). The ambient temperature needs to be maintained between 20 – 22 °C. When the temperature falls outside the above mentioned guidelines it may affect TEWL, skin hydration and skin surface pH measurements (Treffel *et al*., 1994).

2.11.2.5 Skin cleansing

Skin cleansing is an important concept as it is done daily and even the usual usage of water and soaps may influence the skin surface parameters (Schmid and Korting, 1995). It is known that skin cleansing affects the skin surface pH specifically. There is an increase in skin surface pH when washing with alkaline soaps and a decrease in skin surface pH when washing with an acidic type of soap (Parra and Paye, 2003; Schmid and Korting, 1995). New acidic syndets are used frequently, which is more acidic than normal soaps and restores the acidic pH of the skin surface faster than normal soaps (Schmid and Korting, 1995).

In a study done by Schmid-Wendtner and Korting (1995) it was found that when washing ones hands with normal soap it increased the skin surface pH with three units. Water has an effect on the skin surface pH even without the use of soaps. This temporary skin cleansing method only affects the uppermost layer of the stratum corneum and disappears after a few hours. Even though the effect of skin cleansing is temporary it is necessary to eliminate this as a factor during an experimental research study. Deodorant and other topically applied lotions also affect the skin surface pH for a few hours (Parra and Paye, 2003). Rippke *et al*. (2002) stated that when washing ones hands with soap there is not only an increase in skin surface pH, but also an increase in the TEWL indicating impairment of the barrier function.

Gfatter *et al*. (1997) found contradicting results when measuring the skin hydration and the effect of skin cleansing thereon. The only soap having an influence on the skin hydration is alkaline soaps (Gfatter *et al*., 1997).

2.11.2.6 Smoking

Inhalation of tobacco smoke causes a decrease in blood flow in the capillaries (where heat exchange take place) and a decrease in skin temperature changes the sweat gland activity, therefore, affecting skin surface pH. Inhalation of cigarette smoke also leads to an increase in wrinkles and a loss of skin tone. A decrease in collagen decreases the mechanical strength of the skin surface leading to impaired barrier function (Koh *et al*., 2002).

This impaired barrier function as a result of tobacco use makes the skin surface more susceptible to possible pathogens, which affects the skin surface's acidic enzyme as well as resident micro flora and in effect influences the skin surface pH. This impaired barrier function is an indication of a dehydrated stratum corneum and it is illustrated through the measurement of low hydration values (Rippke *et al*., 2002).

2.11.2.7 Caffeine intake

Caffeine intake stimulates the central nervous system. The increase of caffeine leads so increased alertness, attention span, and the level of skin conductance leading to the activation of sweat gland activity (Bruce *et al*., 1986). As there is an increase in sweat gland activity it leads to an increase in skin surface pH values as fewer ions are absorbed (Kleesz, 2012).

2.12 Conclusion

Several barrier creams are used in the workplace as a preventative measure to ensure that the worker is protected against possible allergens or irritants found in the workplace. The main controversy, however, is that different barrier creams may have different effects on the skin barrier function and in some instances even increase the susceptibility of the skin to penetration by chemicals or irritants. The controversy needs to be further investigated, through testing barrier creams that are used specifically in the industry. There are several parameters that are used to indicate the integrity of the barrier function and these include TEWL, skin hydration and skin surface pH. Skin thickness forms part of the total stratum corneum's barrier function and several of the ingredients found in moisturisers may affect the skin thickness through hydration of the corneocytes which in turn will have an impact on skin thickness. Therefore, skin thickness will be measured seperately and considered as a factor on its own. Several intrinsic and extrinsic factors may influence the values of these different parameters and need to be closely regulated or eliminated when measurements are taken.

2. 13 References

Agache P. (2004) The human skin: An overview. *In* Agache P, Humbert P, *eds*. Measuring the skin. Springer. p. 3-28. ISBN 3 540 01771 2.

Agner T, Held E. (2002) Skin protection programmes. Contact Dermatitis; 47: 253-256.

Alvarez MS, Brown LH, Brancaccio RR *et al*. (2001) Are barrier creams actually effective? Curr Allergy Asthma Reports; 1: 337-341.

Alanen E, Nuutinen J, Nicklén *et al*. (2004) Measurement of hydration in the stratum corneum with the moisturemeter and comparison with the corneometer. Skin Res Technol; 10: 32-37.

Baur X, Chen Z, Allmers H *et al*. (1998) Result of wearing test with two different latex gloves with and without the use of skin-protection cream. Allergy; 53: 441-444.

Behne M, Barry N, Hanson K *et al*. (2003) Neonatal development of the stratum corneum pH gradient: localisation and mechanisms leading to emergence of optimal barrier function. Invest Dermatol; 120: 998-1006.

Berardesca E, Pirot E, Singh M *et al*. (1998) Differences in stratum corneum pH gradient when comparing white caucasian and black African-American skin. Br J Dermatol: 139: 855-857.

Berndt U, Wigger-Alberti W, Gabard B *et al*. (2000) Efficacy of a barrier cream and its vehicle as protective measure against occupational irritant contact dermatitis. Contact Dermatitis; 42: 77-80.

Berthaud F, Boncheva M. (2011) Correlation between the properties of the lipid matrix and the degrees of integrity and cohesion in healthy human stratum corneum. Exp Dermatol; 20: 255-262.

Bos. (1997) The skin as an organ of immunity. Clin Exp Immunol; 107: 3-5.

Bruce M, Scott N, Lader M *et al*. (1986) The psychopharmacological and electrophysiological effects of single doses of caffeine in healthy human subjects. Br J Clin Pharmacol; 22: 81-87.

Chew AL, Maibach HI. (2003) Occupational issues of irritant contact dermatitis. Int Arch Occup Environ Health; 76: 339-346.

Courage and Khazaka Electronic GmbH. (2008) Information and operating instructions for Derma Unit SSC3 Sebumeter®/ Corneometer®/ Skin-pH-Meter® and the software for Windows®. Germany:CK

Crosera M, Bovenzi M, Maina G *et al*. (2009) Nanoparticle dermal absorption and toxicity: A review of the literature. Int Arch Occup Environ Health; 82: 1043-1055.

Crowther JM, Sieg A, Blenkiron P *et al*. (2008) Measuring the effects of topical moisturisers on changes in stratum corneum thickness, water gradients and hydration *in vivo*. Br J Dermatol; 159: 567-577.

Darlenski R, Sassning S, Tsankov N *et al*. (2009) Non-invasive *in vivo* methods for investigation of the skin barrier physical properties. European J Pharm Biopharm; 72: 295-303.

Deflin Technologies Ltd. (2010) User's manual, Wireless Vapometer,. P1-39. Denda M. (2000) Skin barrier function as a self-organizing system. Forma; 15: 227-232.

De Paepe K, Desee MP, Rpteeuw D *et al*. (2000) Claim substantiation and efficiency of hydrating body lotions and creams. Contact Dermatitis; 42: 227-234.

Drexler H. (2003) Skin protection and percutaneous absorption of chemical hazards. Int Arch Occup Environ Health; 76: 359-361.

Du Plessis J, Stefaniak A, Eloff F *et al*. (2013) International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: Part 2. transepidermal water loss and skin hydration. Skin Res Technol; 19: 265-278.

Eberlein-König B, Schäfer T, Huss-Marp J *et al*. (2000) Skin surface pH, stratum corneum hydration, trans-epidermal water loss and skin roughness related to atopic eczema and skin dryness in a population of primary school children. Acta Derm Venereol; 80: 188-191.

Egawa M, Tagami H. (2008) Comparison of the depth profiles of water and water-binding substances in the stratum corneum determined in vivo by raman spectroscopy between the cheek and volar forearm skin: effects of age, seasonal changes and artificial forced hydration. Br J Dermatol; 158: 251-260.

Ehlers C, Ivens UI, Moller ML *et al*. (2001) females have lower skin surface pH than men. a study on the influence of gender, forearm site variation, right/left difference and time of day on the skin surface pH. Skin Res Technol; 7: 90-94.

Farahmand S, Tien L, Hui X *et al*. (2009) Measuring transepidermal water loss: a comparative *in vivo* study of condensed-chamber, unventilated-chamber and open chamber systems. Skin Res Technol; 15: 392-398.

Fluhr JW, Dickel H, Kuss O *et al*. (2002) Impact of anatomical location on barrier recovery, skin surface pH and stratum corneum hydration after acute barrier disruption. Br J Dermatol; 146: 770-776.

Fluhr JW, Darlenski R, Berardesca E *et al*. (2008) Ethnic groups and sensitive skin: two examples of special populations in dermatology. Drug Disc Today Disease Mechanisms; 5: 249-263.

Gfatter R, Hackl P, Braun F *et al*. (1997) Effects of soap and detergents on skin surface pH, stratum corneum hydration and fat content in infants. Dermatology; 195: 258-262.

Grice K, Sattar H, Baker H *et al*. (1976) The effect of ambient humidity on TEWL. J Invest Dermatol; 58: 343-346.

Harmsze AM, Houte Mv, Deneer VH *et al*. (2008) Exercise-induced sweating in healthy subjects as a model to predict a drug's sweat-reducing properties in hyperhydrosis: a prospective, placebo-controlled, double blind study. Acta Derm Venereol; 88: 108-112.

Held E, Sveinsdóttir S, Agner T *et al*. (1999) Effect of long-term use of moisturiser on skin hydration, barrier function and susceptibility to irritants. Acta Derm Venereol; 79: 49-51.

Held E, Agner T. (2001) Effect of moisturisers on skin susceptibility to irritants. Acta Derm Venereol; 81: 104-107.

Imhof RE, De Jesus MEP, Xiao P *et al*. (2009) Closed-chamber transepidermal water loss measurement: microclimate, calibration and performance. Int J Cos Sci; 31: 97-118.

Kalia YN, Alberti I, Sekkat N *et al*. (2000) Normalisation of stratum corneum barrier function and transepidermal water loss *in vivo*. Pharm Res; 17: 1148-1150.

Kleesz P, Darlenski R, Fluhr J. (2012) Full-body skin mapping for six biophysical parameters: baseline values at 16 anatomical sites in 125 human subjects. Skin Pharmacol Physiol; 25: 25-33.

Koh J, Kang H, Choi S *et al*. (2002) Cigarette smoke associated with premature facial wrinkling: image analyses of facial skin replicas. Int J Dermatol; 41: 21-27.

Korinth G, Weiss T, Penkert S *et al*. (2007) Percutaneous absorption of aromatic amines in rubber industry workers: impact of impaired skin and skin barrier creams. Occup Environ Med; 64: 366-372.

Korinth G, Lüersen L, Schaller KH *et al*. (2008) Enhancement of percutaneous penetration of aniline and *o*-toluidine *in vitro* using barrier creams. Toxicology; 22: 812-818.

Kresken J, Klotz A. (2003) Occupational skin-protection products – a review. Int Arch Occup Environ Health; 76: 355-358.

Kreyden OP, Scheidegger EP. (2004) Anatomy of the sweat glands, pharmacology of botulinum toxin, and distinctive syndromes associated with hyperhidrosis. Clin Dermatol; 22: 40-44.

Lambers H, Piessens S, Bloem A *et al*. (2006) Natural skin surface pH is on average below 5, which is beneficial for its resident flora. Int J Cosmetic Sci; 28: 359-370.

Larson E. (2001) Hygiene of the skin: when is clean to clean? Emerg Infect Diseases; 7: 225-228.

Levin J, Maibach H. (2005) The correlation between transepidermal water loss and percutaneous absorbtion: an overview. J Control Release; 103: 291-299.

Lodén M, Andersson AC, Lindberg M *et al*. (1999) Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (Canoderm®). Br J Dermatol; 140: 264-267.

Madison K. (2003) Barrier function of the skin: “La Raison d’Être” of the epidermis. J Invest Dermatol; 121: 231-241.

Nixon R, Roberts H, Frowen K *et al*. (2006) Knowledge of skin hazards and the use of gloves by Australian hairdressing students and practicing hairdressers. Contact Dermatitis; 54: 112-116.

Parra JL, Paye M. (2003) EEMCO guidelines for the *in vivo* assessment of skin surface pH. Skin Pharmacol Appl Skin Physiol; 16: 188-202.

Proksch E, Brasch J. (2011) Contact Dermatitis. *In* Proksch E, Brash J, *eds*. Role of the permeability barrier in contact dermatitis. Springer. P. 121-135. ISBN. 987 3 642 03826 6.

Rippke F, Schreiner V, Schwanitz HJ. (2002) The acidic milieu of the horny layer. Am J Clin Dermatol; 3: 261-272.

Rippke F, Schreiner V, Doering T *et al*. (2004). Stratum corneum pH in atopic dermatitis: Impact on skin barrier function and colonization with Staphylococcus aureus. Am J Clin Dermatol; 5: 217-223.

Rogers J, Harding C, Mayo A *et al*. (1996) Stratum corneum lipids: the effect of ageing and the seasons. Arch Dermatol Res; 288: 265-770.

Schmid MH, Korting HC. (1995) The concept of the acid mantle of the skin: its relevance for the choice of skin cleansers. Dermatology; 191: 276-280.

Schmid-Wendtner MH, Korting HC. (2006) The pH of the skin surface and its impact on the barrier function. Skin Pharmacol Physiol; 19: 296- 302.

Spencer TS, Linamen CE, Akers WA *et al*. (1975) Temperature dependence of water content of stratum corneum. Br J Dermatol; 93: 159-164.

Stefaniak A, Du Plessis J, John S *et al*. (2013) International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: part 1. pH. Skin Res Technol; 19: 59-68.

Tagami H, Ohi M, Iwatsuki K *et al*. (1980) Evaluation of skin surface hydration *in vivo* by electrical measurement. J Invest Dermatol; 75: 500-507.

Treffel P, Panisset F, Faivre B *et al*. (1994) Hydration, tranepidermal water loss, pH and skin surface parameters: correlations and variations between dominant and non-dominant forearms. Br J Dermatol; 130: 325-328.

Ushio H, Nohara K, Fujimaki H *et al*. (1999) Effect of environmental pollutants on the production of pro-inflammatory cytokines by normal human dermal keratinocytes. Toxicol Lett; 105: 17-24.

Verdier-Sévrain S, Bonté F. (2007) Skin hydration: a review on its molecular mechanisms. J Cosmet Sci; 6: 75-82.

Waller JM, Maibach I. (2005) Age and skin structure and function, a quantitative approach (I): blood flow, pH, thickness, and ultrasound echogenicity. Skin Res Technol; 11: 221-235.

Yosipovitch G, Xiong GL, Haus E *et al.* (1998) Time-dependent variations of the skin barrier function in humans: transepidermal water loss, stratum corneum hydration, skin surface pH and skin temperature. J Invest Dermatol; 110: 20-23.

CHAPTER 3: Article

3.1 Instructions to authors

This article was written according to the instructions for authors of an accredited journal namely, *Annals of Occupational Hygiene* for possible publication purposes.

- ***Language****:*
  British styles and spelling was used and words or phrases which might be unclear in other parts of the world was avoided or clearly explained. This article was edited for language before submission.

- ***Brevity:***
  The necessary length of the paper depended on the subject, but any submission was as brief as possible consistent with clarity. The number of words, excluding the abstract, references, tables and figures, was stated as a message to the Editor at the time of submission. The length of the paper should be not more than 5000 words.

- ***Structure:***
  This manuscript conformed to the following pattern: Introduction, Methods, Results, Discussion, and Conclusions. The paper was prefaced by an abstract of the argument and findings, which may also be arranged under the same headings.

- ***Units and symbols:***
  SI units were used**,** though their equivalent in other systems was given as well.

- ***Figures:***
  Computer-generated graphics should be reproduced in grey-scale if they are to be published in black and white.

- ***Tables*****:**
  Tables were numbered consecutively and given a suitable caption. As with Figures, it is helpful to incorporate them into the text of the first submission, but in the revised version each table should be presented on a separate page. Footnotes to tables were provided below the table and were referred to by superscript lowercase letters.

- **References:**

  References were included in this paper if they were essential in order to develop an argument, hypothesis. Referencing used in the text was done in the form of Jones (1995), Jones and Brown (1995) or Jones *et al*. (1995) if there were more than two authors. They were incorporated into the text and the following is an example: Jones and Brown (1995) and Horpes *et al*. (2006) observed that there is a difference between the two factors.

- At the end of the paper, references were listed in alphabetical order by name of first author, using the Vancouver Style of abbreviation and punctuation. An ISBN was given for books and other publications where appropriate.

Short-term effects of selected barrier creams on skin barrier function

Authors: A Vermaak, CJ Van der Merwe, FC Eloff

Affiliations*:* Subject Group Physiology, North-West University, Private Bag x6001, Potchefstroom, South Africa.

Corresponding author: A Vermaak, Subject Group Physiology, North-West University, Private Bag x6001, Potchefstroom, South Africa.

Word Count: 5073

3.2 Abstract:

Background: Barrier creams are used in the workplace environment and applied to the skin surfaces of workers that are frequently exposed to irritants and allergens which include the face, neck and hands. The purpose of barrier creams is to prevent the development of irritant contact dermatitis and contact dermatitis by preventing the penetration of irritants and allergens through the skin surface. Differences exist in the literature concerning the following: the mechanism of action of barrier creams, different types of barrier creams, substances they afford protection against, differences in skin surface properties between racial groups and the effect that barrier creams have on the skin surface parameters. In light of the above, it is clear that, barrier creams and the effect they exert on the skin surface need further investigation.

Aim: The aim of this study was to describe the effect of barrier creams on the skin barrier function, using skin surface parameters. These parameters included: TEWL (transepidermal water loss), skin surface hydration and skin surface pH. Total skin thickness was assessed and evaluated as a variable on its own.

Method: Forty two non-smoking participants were included and tested in this study, of which 21 were African and the rest Caucasian. TEWL, skin hydration and skin surface pH were used to evaluate the differences in the effect of two different barrier creams (Reinol Solvgard and Momar Chex) on skin barrier function. TEWL was measured by making use of a closed chamber Vapometer (Deflin Technology Ltd., Kuopio, Finland), skin hydration using a Corneometer® CM 825 and skin surface pH using a pH meter probe (Courage and Khazaka Electronic Köln, Germany).

A micro-pipette was used to drip a standard volume of 20 µl of ultrapure water on the skin surface before the researcher placed the pH meter probe onto the skin surface. Total skin thickness was measured by making use of ultrasound (Ultrascan 22 - TBS0061B) (Courage and Khazaka Electronic Köln, Germany). Three consecutive measurements were taken on the mid-forearm and the palm of the experimental arm. After baseline values were measured, 5 ml of the selected barrier cream was applied to the experimental arm. The barrier cream (selected for the day) was reapplied after 2, 4 and 6 hours and measurements were taken after 2, 4, 6 and 8 hours. The total skin thickness was measured at time zero and at 8 hours.

Results:

*TEWL***:** For both barrier creams, statistical significant differences ($p \leq 0.05$) were found between TEWL on the palms of African participants and Caucasian participants.

Skin hydration: Statistical significant differences ($p \leq 0.05$) were obtained with regard to mid-forearm skin hydration when comparing Reinol Solvgard with Momar Chex (this was applicable to both racial groups). A statistical significant difference ($p \leq 0.05$) was obtained with regard to mid-forearm skin hydration when comparing African participants with Caucasian participants (this was only applicable to Reinol Solvgard). Statistical significant differences ($p \leq 0.05$) were obtained with regard to palm skin hydration when comparing Reinol Solvgard with Momar Chex (this was applicable to both racial groups). Statistical significant differences ($p \leq 0.05$) were obtained with regard to skin hydration palm when comparing African participants with Caucasian participants (this was applicable to both barrier creams).

Skin surface pH: A statistical significant difference ($p \leq 0.05$) was obtained with regard to the pH of the mid-forearm when comparing Reinol Solvgard with Momar Chex (this was applicable to only the African participants). A statistical significance ($p \leq 0.05$) was obtained with regard to skin surface pH mid-forearm when comparing African participants with Caucasian participants (this was applicable to Momar Chex barrier cream only). A statistical significant difference ($p \leq 0.05$) was obtained with regard to the pH of the palm when comparing Reinol Solvgard with Momar Chex (this was only applicable to the African racial group).

Conclusion: It was evident when assessing the effect that barrier creams have on the different skin surface parameters that the following conclusion could be made: Momar Chex barrier cream indicated to have more positive effects when compared to the Reinol Solvgard barrier cream. This may be ascribed to the fact that both barrier creams lowered TEWL (positive effect), Reinol Solvgard decreased skin hydration (negative effect) whereas, Momar Chex increased the skin hydration (positive effect) and lastly both barrier creams increased skin surface pH (negative effect). Furthermore, the following were observed:

- There were short-term changes (over a period of 8 hours) or effects on the skin surface parameters after the application of barrier creams.
- Differences were observed between two barrier creams and between the two racial groups.

Therefore, it may be concluded that the objectives of this research study was reached.

Keywords: TEWL, skin surface hydration, skin surface pH, Reinol Solvgard barrier cream, Momar Chex barrier cream, racial groups, skin barrier function.

3.3 Introduction

Occupational exposure to various substances may occur through three different pathways which include oral ingestion, inhalation and dermal exposure. The field of occupational hygiene has historically focused on inhalation as the major route of exposure. Different techniques have been developed in order to measure the level of inhalation exposure. The focus has however, begun to shift with more research being done on dermal exposure. Dermal exposure may occur through different ways which include direct skin contact with air contaminants, transfer through contaminated surfaces and lastly the clothes that a worker wears which may influence the rate of absorption (Schneider *et al*., 2000).

The main barriers through which hazardous substances may penetrate are the clothes worn by the workers (that forms a physical barrier) and the stratum corneum layer of the skin. There are different factors that determine the rate of diffusion through the skin surface and they include the concentration of the substance, exposure time to the contaminant and type of clothes worn (Schneider *et al*., 2000). As a result of dermal exposure to several hazardous substances and the detrimental effects that they may have, several control measures have been implemented to prevent or to limit exposure of which barrier creams are one of the PPE (Personal Protective Equipment) (Agner and Held, 2002; Brown, 2004).

Barrier creams, also known as skin protection creams, are used in the industry to prevent penetration of harmful substances through the skin surface or otherwise to prevent the occurrence of contact dermatitis (Wigger-Alberti *et al*., 1999; Berndt *et al*., 2000). According to Wigger-Alberti *et al*. (1999), the value of barrier creams in the work setting is greatly questioned. The mechanism of action of barrier creams remain controversial with, different mechanisms having been proposed. It is known that oil-repellent (water-based) barrier creams protect against organic solvents and oil-based types of substances, whereas water-repellent (oil-based) barrier creams protect against acids, alkalis and soaps. Another mechanism of action is that fatty amine amide acetate binds to the carboxyl groups of keratin which are negatively charged, whilst the ammonium ion that is positively charged binds with the epidermis which has a negative charge. This mechanism creates a second layer that prevents the penetration of substances through the epidermis. Some of the additional ingredients include chelating agents, talcum, zinc oxide and tanning substances that bind to metal ions or reduces the penetration of external stressors through the epidermal layer of the skin (Wigger-Alberti *et al*., 1999).

The epidermal layer of the skin surface is of great importance as hazardous substances may penetrate this layer, leading to irritation of the dermal layer, sensitisation in some individuals and even toxic effects (Drexler, 2003). Several parameters may be used to evaluate the effect of barrier creams on skin barrier function, and the integrity of the barrier. These parameters include TEWL, skin hydration and skin surface pH. Skin surface parameters can be used to evaluate the effect of barrier creams on the skin barrier function. TEWL is the amount of insensible water loss through the skin surface. The desired effect of the barrier creams would be a decrease in TEWL however, some barrier creams have been known to increase TEWL. Skin hydration is one of the parameters used to indicate if the stratum corneum is either in a dehydrated or a hydrated state. There are several lotions and protective creams manufactured with the aim of hydrating the stratum corneum. Moisturisers that increase the skin hydration is the desired effect. Skin surface pH is the negative logarithm of the concentration of hydrogen ions in the watery solution of the stratum corneum. Normal skin surface pH range between 4 – 6 however, the skin surface pH of the stratum corneum tends to be more acidic. This acidic skin surface pH creates a favourable environment for residential flora and their functioning. An increase in skin surface pH may affect the residential flora of the skin surface and promote the penetration of external microbes through the skin surface (Drexler, 2003; Lambers *et al*., 2006).

The above mentioned parameters need to be carefully measured if they are to be used to assess the condition of the skin and the state of the skin barrier function. During skin surface measurements, all the factors that may influence the skin surface parameters need to be eliminated or greatly reduced in order to focus only on the effect that barrier creams have on the skin surface. These factors are divided into three main groups, including endogenous factors, exogenous factors and experimental factors (Parra and Paye, 2003). Endogenous factors include anatomical site, gender, age, race, dominant versus non-dominant forearm, circadian rhythms, sweating and skin temperature. Exogenous factors include cleansing habits and the application of topical products, relative humidity and ambient temperature. There are a few experimental factors linked to the instrument (pH meter) that may have an effect on the skin surface pH and includes, electrolyte-liquid level of the pH meter, contamination of the electrode, excess water on the electrode and a dry electrode (Parra and Paye, 2003).

The mechanism of action of barrier creams and the effect that they elicit on the barrier function are controversial (Alvarez *et al*., 2001).

This controversy needs to be further investigated through testing the short-term effects that barrier creams have over a total period of 8 hours. The two barrier creams that will be included in this study are Momar Chex and Reinol Solvgard barrier creams. As there are differences between African and Caucasian skin there may be a difference in the effect that barrier creams have on these racial groups (Berardesca *et al*., 1998). This controversy will be investigated in this particular research.

The specific objectives of this study will include:

- The short-term[3] effects that selected barrier creams have on barrier function and skin thickness of African skin in comparison with Caucasian skin.
- To compare Momar Chex barrier cream with Reinol Solvgard barrier cream using identical skin surface parameters (TEWL, skin hydration and skin surface pH).
- How different skin surface parameters are affected over a total time period of 8 hours for both barrier creams.

Note 3: The words short-term are used in this study as each barrier cream is only tested over a period of 8 hours and not tested over a long term period of months or years.

3.4. Method

3.4.1 Instrumentation

Three skin surface parameters were selected and used to evaluate the barrier function of the skin. These parameters were TEWL, skin hydration and skin surface pH. Furthermore, these parameters were also used to indicate the short-term effect that two selected barrier creams have on the skin barrier function over a time period of 8 hours.

TEWL was measured using a closed chamber Vapometer (Deflin Technology Ltd., Kuopio, Finland). Skin hydration was measured with a Corneometer® CM 825 and skin surface pH with a pH meter probe (Courage and Khazaka Electronic Köln, Germany). The corneometer and pH meter probe (Courage and Khazaka Electronic Köln, Germany) were connected to the multi probe adapter (MPA) (Courage and Khazaka Electronic Köln, Germany). The MPA was also attached to sensors that recorded the relative humidity and ambient room temperature in the laboratory throughout the entire research study. A micro pipette was used to drip a standard volume of 20 µl ultrapure water on the surface of the skin, before the electrode of the pH meter probe was placed on the skin surface.

Total skin thickness was also measured to evaluate the effect that the barrier creams may have on total skin thickness. The instrument used for this was the Ulstrascan 22 - TBS0061B from Courage and Khazaka Electronic Köln, Germany. Total skin thickness values were recorded in millimetre (mm).

3.4.2 Barrier creams

A questionnaire regarding the use of barrier creams in the industry was circulated to members of the Southern African Institute for Occupational Hygiene (SAIOH), the professional body for occupational hygiene professionals in Southern Africa. The purpose of the questionnaire was to identify popular barrier creams currently used in the South African industry to ensure the inclusion thereof in the research. The two barrier creams included in the research were Momar Chex and Reinol Solvgard barrier creams. Both of these barrier creams are of an oil-repellent nature that can be used to protect the worker against oil-based substances that may penetrate the skin surface. Both barrier creams were tested on each of the participants and the selection of the barrier cream (to be tested on day one) for each of the participants were randomly selected to eliminate the effect that barrier creams may have on one another.

Ultrapure water (deionised water) with a pH of 6.9 was used from the Millipore Purification system as a contact medium during the pH measurements throughout the study. Ultrapure water was used to rinse the electrode after calibration and a standard volume of 20 µl was also placed on the skin surface where the pH measurement was taken.

3.4.3 Participants

A total of 42 male participants participated in this research of which 21 were Caucasian and the rest were African.

Measurements were only conducted after participants understood and provided informed consent by signing an informed consent letter. An example of the informed consent letter is included in the appendix. If there were any signs of skin irritation, lesions or scars present at the anatomical sites to be measured, participants were excluded from the study. Non-smoking participants between 18 and 26 years were selected to participate in the research study.

Furthermore, the participants were not allowed to do any of the following activities if they agreed to participate in the research study:

- Consume any alcohol or caffeine 12 hours before the session.
- Make use of any soaps / moisturisers 12 hours before the session.
- Bath / shower on the day of the study.

3.4.4 Calibration

Both the corneometer and the pH meter were calibrated daily, before the commencement of the measurements. All the instruments were used in accordance with the instructions of the manufacturer. The buffer solutions of the pH meter was kept in a refrigerator and used within a three day period.

3.4.5 Acclimation

The ambient room temperature in the laboratory was regulated between 20 °C and 22 °C by an air conditioning unit. The relative humidity was observed throughout the entire research and had to be within a range of 40 – 60%. The laboratory did not have the means to control the relative humidity and if the relative humidity level fell outside these values no measurements were taken on that day. Each participant was acclimatised in the laboratory for 20 minutes before commencement of the measurements. All of the instruments were also acclimatised to the conditions in the laboratory 20 minutes prior to their use.

3.4.6 Anatomical sites

The experimental arm was selected and the barrier cream was applied. The selection of the experimental arm and the first barrier cream used on day one was randomly selected for each of the participants. The two anatomical sites used for this research included the volar mid-forearm and the palm of the hand.

The mid-forearm used as anatomical site was located by measuring the total length of the forearm by making use of a tape measure. It was measured from the elbow to the wrist and the total length was divided by two. The site was marked through the use of a marker pen and four dots were made of approximately 2 cm from one another to form a perimeter.

For every surface parameter, the probes were placed inside the perimeter and the measurements were taken on the same area to ensure that the obtained data was comparable.

For the location of the measurement site on the palm, a line was drawn from between the index and middle finger to where these lines crossed horisontally with the base of the thumb. This area was marked with a marker pen by using four dots that were approximately 2 cm from one another to form a perimeter and the probes were then placed inside the perimeter area.

Three consecutive measurements were taken on both the volar mid-forearm and the palm of the experimental arm for each of the parameters and at each time interval (0, 2, 4, 6 and 8 hours).

Total skin thickness was measured on the volar mid-forearm and palm only at time zero and at 8 hours. The mean of the three measurements was calculated at every time interval and for each of the different parameters.

3.4.7 Application procedure of barrier creams

After participants acclimatised and the anatomical sites were marked, the baseline values were measured. Baseline values refer to measurements that were recorded before the barrier cream was applied and which served as a reference. TEWL was measured after which skin hydration, skin surface pH and total skin thickness followed. This sequence was used throughout the study.

The researcher that applied the barrier cream wore Nitrile gloves to prevent contamination. Five millilitres (ml) of the barrier cream were measured using a measuring spoon. The researcher applied the barrier cream evenly on the entire experimental arm starting from the elbow towards the forearm (and the back of it), between the fingers and ending at the tips of the fingers. The excess barrier cream was removed by making use of a paper towel.

The measurements procedure was repeated every 2, 4, 6 and 8 hours before barrier creams were re-applied. The barrier cream was re-applied at 2, 4 and 6 hours. Total skin thickness however, was only measured at time zero (baseline) and at 8 hours.

3.4.8 Ethical aspects

The project was approved by the Ethical committee of the North-West University (Potchefstroom Campus) prior to the commencement of the research. The following ethical number was given by the NWU Ethics Committee: NWU-00097-10-55

3.5 Statistical Analysis

Statistica 11.0 (Statsoft Inc.) was used to plot histograms in order to determine whether data were normally distributed. Most of the data were not normally distributed and therefore, were logged transformed so that they could be used in further analysis.

The experimental arms' base line values (which served as a control before the barrier creams were applied) and measurement values (2, 4, 6 and 8 hours) were used for statistical analysis.

Independent t-tests by groups were used to test for a statistical significant difference between each of the parameters at the specific time intervals, but mainly used to indicate the difference between the two barrier creams and between the two racial groups. Data differences with *p*-value of ≤ 0.05 were considered as statistically significant. Independent t-tests that indicated means of, and *p*-values between the different groups are provided in table format in the appendix. It was decided to make use of repeated measures (ANOVA) to indicate whether there was a statistical significant difference over a period of 8 hours between the racial groups (African versus Caucasian) and the barrier creams (Momar Chex versus Reinol Solvgard). The *p*-values were used to indicate changes over the total time period of 8 hours and not used as a mean at any specific time interval. Graphpad Prism (version 6.05) was used to illustrate these repeated measures by making use of line graphs to illustrate visually changes over a time period of 8 hours which represented a normal workday shift.

For the ease of the reader the following should be noted:

- For comparison of barrier creams the groups were divided by race:
    1. Reinol Solvgard barrier cream compared to Momar Chex barrier cream (African racial group).
    2. Reinol Solvgard barrier cream with Momar Chex barrier cream (Caucasian racial group)
- For comparison of racial groups was divided by barrier creams:
    1. African racial group compared to Caucasian racial group (Reinol Solvgard barrier cream).
    2. African racial group compared to Caucasian racial group (Momar Chex barrier cream).

3.6. Results

Line graphs were used to illustrate changes in skin surface variables over time.

Figures 1 – 3 contain both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for TEWL, skin hydration and skin surface pH for both anatomical sites (mid-forearm and palm).

Figures 1 (a) and 1 (b) follow to illustrate the effect that two barrier creams had on TEWL over a period of 8-hours.

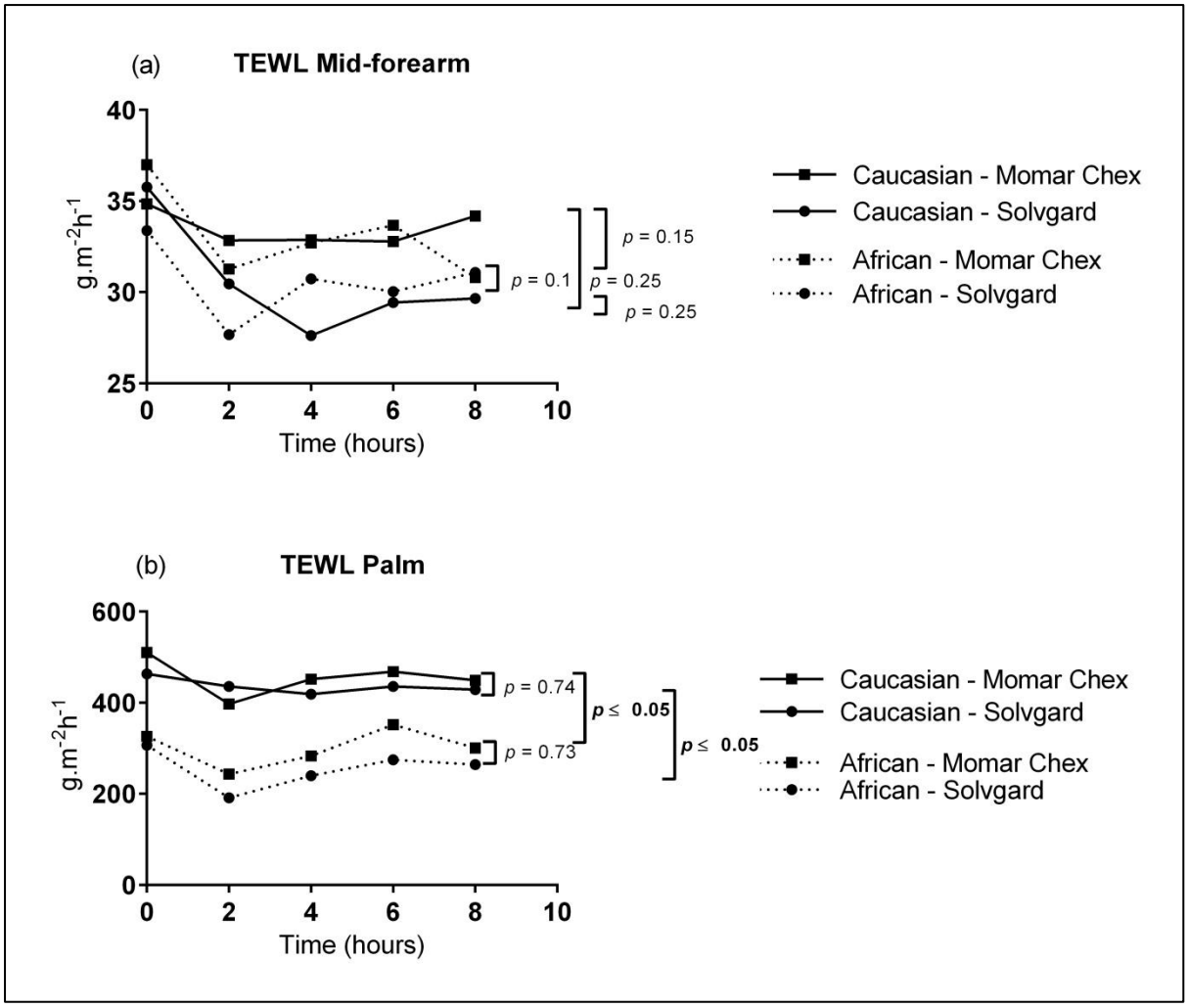


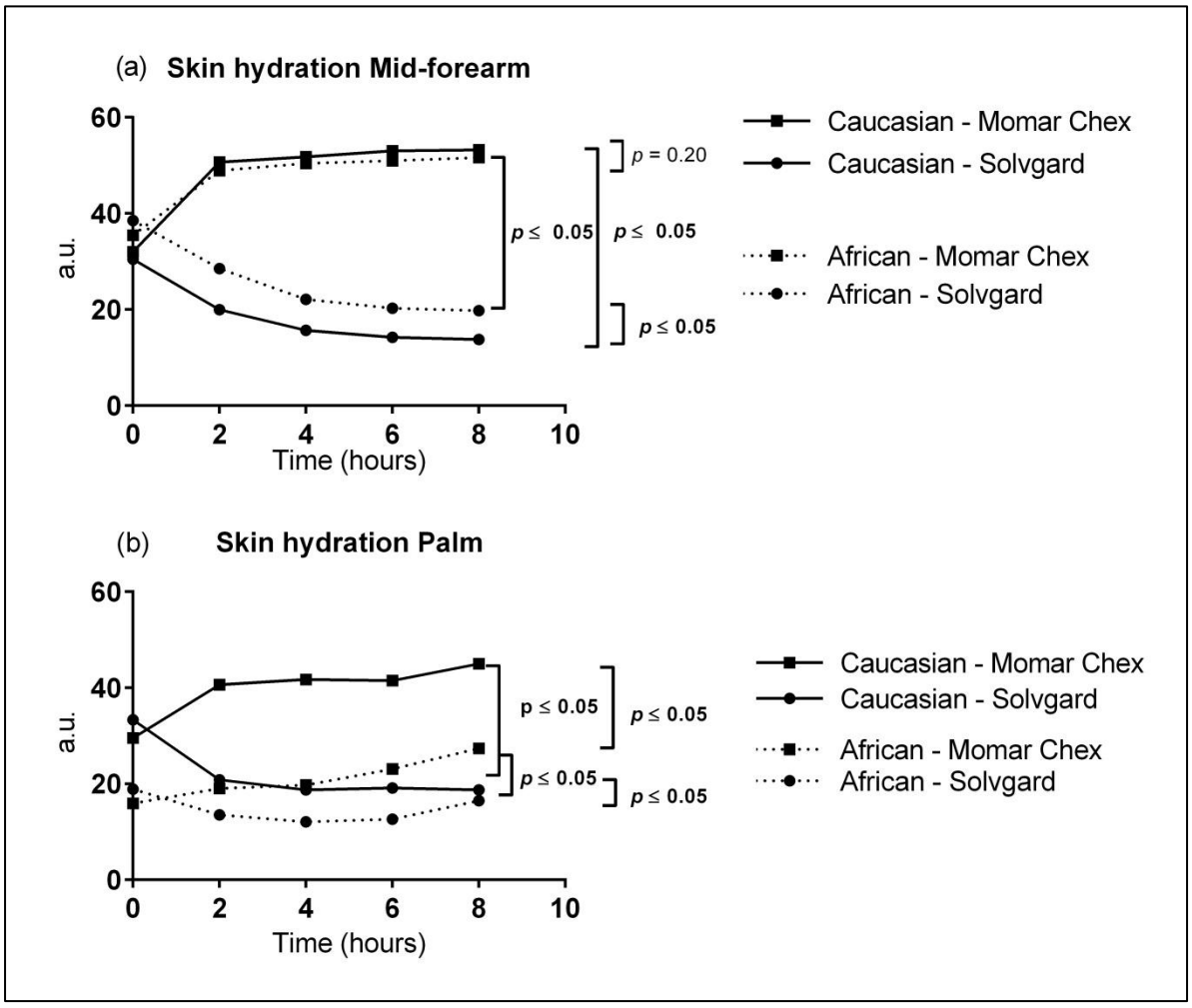
Figure 1: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for TEWL for both anatomical sites (mid-forearm and palm).

As may be gathered from Figures 1 (a) and 1 (b) there were decreases observed in TEWL over an 8-hour time period for both racial groups (African and Caucasian), barrier creams and anatomical sites. Furthermore, Figure 1 (b), which represents the palm of the hand, indicated overall higher TEWL values when compared to the mid-forearm (see Figure 1(a)).

Figure 1 (a) illustrated no significant differences with regards to TEWL mid-forearm when assessing changes between Reinol Solvgard and Momar Chex (this applied to both racial groups). No significant differences were illustrated (see Figure 1 (a)) with regards to TEWL mid-forearm when comparing African participants with Caucasian participants (this applies to both barrier creams). In conclusion no significant differences were observed in Figure 1(a).

Statistical significant differences ($p \leq 0.05$) were illustrated (see Figure 1 (b)) with regards to TEWL palm when comparing African participants with Caucasian participants (this applies to both of the barrier creams). In contrast, no significant differences were illustrated when comparing Reinol Solvgard barrier cream with Momar Chex barrier cream (this applies to both of the racial groups).

Figures 2 (a) and 2 (b) follow to illustrate the effect that two barrier creams had on skin hydration over a period of 8-hours.



a.u. *arbitrary unit*

Figure 2: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for skin hydration for both anatomical sites (mid-forearm and palm).

As gathered from Figures 2 (a) and 2 (b) there was both a steep increase and decrease in skin hydration levels depending on the barrier cream assessed. It was evident that Momar Chex barrier cream increased the skin hydration, whereas the Reinol Solvgard barrier cream decreased the skin hydration (see Figures 2 (a) and 2 (b). It should be noted that this finding was true for both racial groups and anatomical areas.

Figure 2 (a) illustrated statistical significant differences ($p \leq 0.05$) with regards to skin hydration mid-forearm comparing Reinol Solvgard with Momar Chex barrier cream (this applied to both racial groups). A statistical significant difference ($p \leq 0.05$) with regards to skin hydration mid-forearm was illustrated (see Figure 2 (b)) when comparing African participants with Caucasian participants (this applies to the Reinol Solvgard barrier cream), whereas no statistical significant difference in data were illustrated when comparing the racial groups (this applies to the Momar Chex barrier cream).

Figure 2 (b) illustrated statistical significant differences ($p \leq 0.05$) with regards to skin hydration palm when comparing Reinol Solvgard with Momar Chex barrier cream (this applies to both barrier creams). In addition, statistical significant differences ($p \leq 0.05$) were observed (see Figure 2 (b)) with regards to skin hydration palm when comparing African participants with Caucasian participants (this applies to both of the barrier creams).

Figures 3 (a) and 3 (b) illustrating the effect that two barrier creams had on skin surface pH over a period of 8-hours.

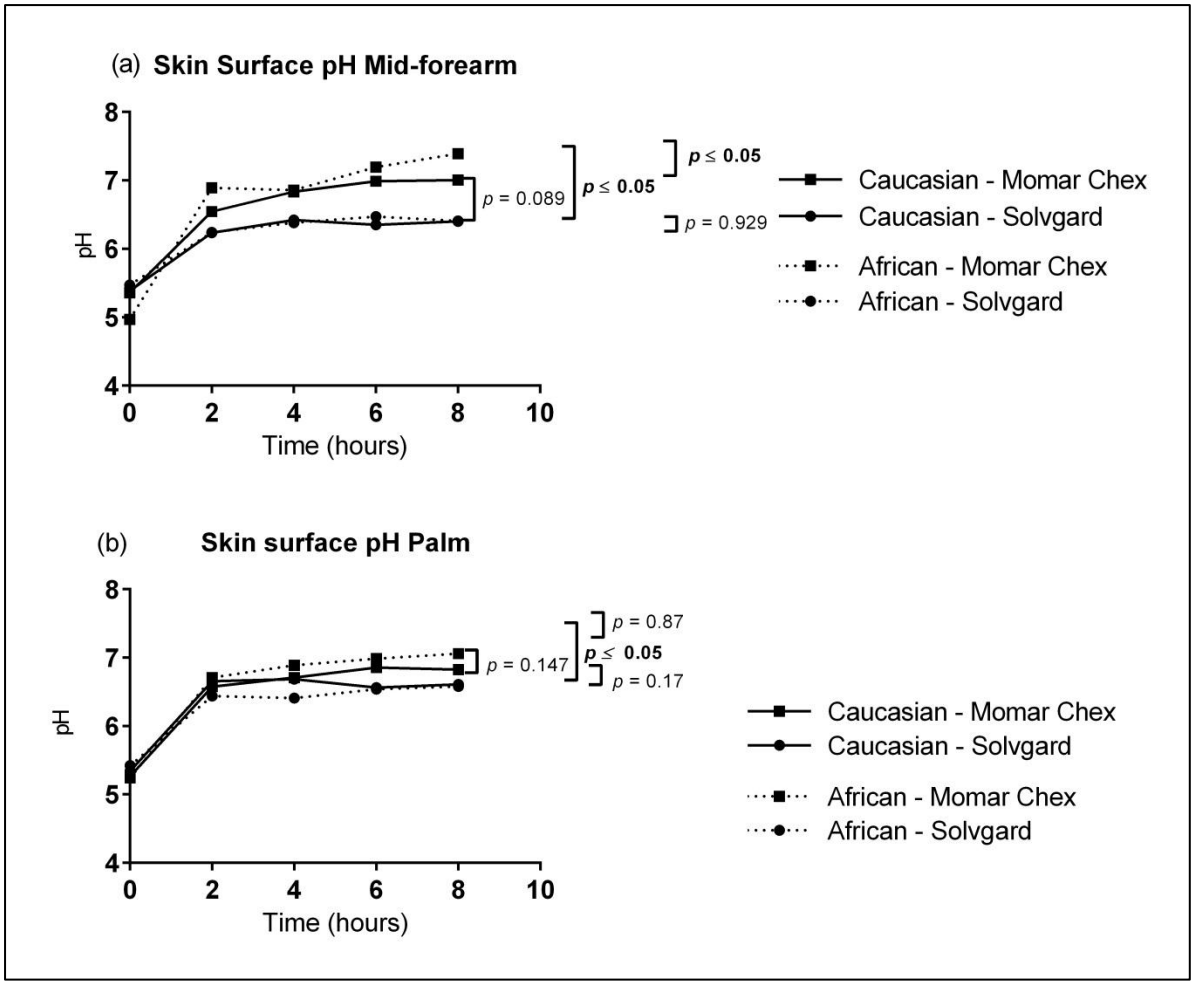


Figure 3: Line graph illustrating both baseline and experimental values (of the experimental arm) obtained from African and Caucasian participants for skin surface pH for both anatomical sites (mid-forearm and palm).

As can be seen from Figures 3 (a) and 3 (b) there was a steep increase in skin surface pH of approximately 2 units for both barrier creams and both of the racial groups. Figure 3 (a) illustrated a statistical significant difference of ($p \leq 0.05$) with regards to skin surface pH mid-forearm when comparing Reinol Solvgard with Momar Chex for the African race, whereas no statistical significant difference was illustrated between the two barrier creams for the Caucasian racial group.

A statistical significant difference ($p \leq 0.05$) was illustrated (see Figure 3 (a)) with regards to skin surface pH mid-forearm when comparing African participants with Caucasian participants for the Momar Chex barrier cream, yet no statistical significant difference was illustrated when comparing the racial groups for the Reinol Solvgard barrier cream.

Figure 3 (b) illustrated a statistical significant difference ($p \leq 0.05$) with regards to skin surface pH palm when comparing Reinol Solvgard barrier cream with Momar Chex barrier cream for the African racial group, yet no statistical significant difference in data were illustrated between barrier creams for the Caucasian racial group. No statistical significant difference in data were illustrated with regards to skin surface pH palm when comparing the two racial groups (this applied to both barrier creams).

3.6.1 Total skin thickness

Total skin thickness was measured at baseline (time zero) and after the 8 hour time period for each of the participants, both arms and for both of the barrier creams. After statistical analysis no statistical significant differences were found for total skin thickness over an 8 hour time period between the two racial groups and barrier creams. Please refer to Table 4 on page 73 for precise values tabled.

3.7 Discussion

3.7.1 Short-term effect of barrier creams on the skin surface parameters:

As can be seen from Figures 1 (a) and (b) there were decreases in TEWL after the application of both barrier creams, for both racial groups and on both anatomical sites. According to current research is the desired effect (Held, 1999; Madison, 2003; Du Plessis *et al*., 2013). In contrast, an increase may have indicated damage to the barrier of the skin with the resultant possibility of increased permeation of substances through the skin surface. There are several controversies in the literature regarding the effect that barrier creams have on TEWL, with some studies indicating that barrier creams decrease TEWL, whereas other studies indicate that barrier creams increase TEWL (Held, 1999; Madison, 2003; Du Plessis *et al*., 2013).

There was a steep increase in skin hydration (see Figures 2 (a) and (b)) for both anatomical sites after the application of Momar Chex barrier cream (this was applicable to both racial groups). Momar Chex barrier cream increased the skin hydration, as previously discussed, which is in accordance with the findings of a study conducted by Yokota and Maibach (2006). Their study confirmed that some barrier creams show this tendency in order to hydrate the stratum corneum layer of the skin.

The fact that the Momar Chex barrier cream increased the skin hydration levels is seen as an advantage of this barrier cream. In contrast to this, the Reinol Solvgard barrier cream decreased the skin hydration. A decrease in water content may lead to cracks in the skin and ultimately to the development of dermatitis (Yokota and Maibach, 2006). Therefore, this may be one of the disadvantages of the Reinol Solvgard barrier cream.

The normal skin surface pH is a topic that has been greatly debated in several literature studies, yet most of the research indicate that the skin surface pH should be between 4 and 6. An acidic skin surface pH is needed for normal bacterial flora and to prevent the penetration of pathogens through the skin surface (Schmid and Korting, 1995; Rippke, 2002). As can be seen in Figures 3 (a) and (b) there was an increase of approximately 2 units in the skin surface pH for both of the barrier creams and racial groups. Increases may indicate a disadvantage of both the barrier creams as an increase in skin surface pH may increase the possibility of penetration of pathogens through the skin surface and interfere with the normal desquamation process (Schmid and Korting, 1995). In addition, increases in pH values may be attributed to circadian rhythms where some studies indicate highest pH values measured in the afternoon however; values were not as high as measured in this study (Rippke, 2002).

3.7.2 Differences between the two barrier creams:

Both barrier creams used in this research are of an oil-repellent nature. There are several controversies regarding the mechanism of action of barrier creams (Alvarez *et al*., 2001). Alvarez *et al*. (2001) stated that different ingredients may explain the mechanism of action of the barrier cream on the skin surface. Although both these barrier creams protect against the penetration of oil-based substances through the skin surface they may elicit different effects on the barrier function due to different ingredients. Reinol Solvgard contains zinc oxide as an ingredient that causes a shielding effect and this may explain the whitish hardening effect of this barrier cream, whereas Momar Chex does not contain this ingredient.

As can be seen from Figures 1 (a) and (b) there was no significant difference between the two barrier creams for both the anatomical areas when using TEWL as an indicator. Both barrier creams therefore, have the same effect on TEWL.

The TEWL values were higher on the palm of the hand when compared to the mid-forearm. This may be due to the fact that the palm of the hand is more prone sweating over the long term when compared to the mid-forearm (Kleesz, 2012).

Even after the participant acclimatised to eliminate sweat as a factor the TEWL on the palm remained elevated when compared to the mid-forearm. Even though there was a difference in the value between these two anatomical areas there was no difference between barrier creams' effect on TEWL for both of the anatomical areas.

As can be seen from Figures 2 (a) and (b) there was a statistical significant difference for skin hydration between the two barrier creams for both the anatomical sites. Reinol Solvgard barrier cream decreased the skin hydration, while Momar Chex increased the skin hydration. Several moisturisers have been developed to increase the stratum corneum hydration to give it a soft smooth texture and to prevent dryness of the skin surface and this effect is in accordance with the Momar Chex barrier cream (increasing skin hydration) (Held *et al*., 1999). The normal stratum corneum has a water content of between 20 and 35% and in the absence of this percentage of water it may lead to cracks in the skin (Yokota and Maibach, 2006). As Reinol Solvgard barrier cream lowers the skin hydration it may in effect dehydrate the stratum corneum layer of the skin surface which is a disadvantage of this specific barrier cream.

A low skin surface pH is needed to afford protection against pathogenic organisms and external microbes. An increase in skin surface pH may indicate alterations in barrier function and a possible occurrence of dermatitis which in that case needs further investigation (Schmid and Korting, 1995; Rippke, 2002). Figure 3 (a) and 3 (b) illustrated a statistical significant difference between the two barrier creams (for both the mid-forearm and palm), yet this phenomenon is only seen when considering the results of the African subjects.
In both instances the Momar Chex barrier cream increased the skin surface pH more when compared to the Reinol Solvgard barrier cream which may be due to the fact that Momar Chex may contain certain ingredients that may increase the skin surface pH. Figures 3 (a) and 3 (b) illustrate no significant difference indicated between the two barrier creams (for both the mid-forearm and palm) when investigating the Caucasian subjects. This may be due to the fact that African skin responds differently to the barrier creams than the Caucasian skin (Fluhr *et al*., 2008). This phenomenon will be discussed further in the next section.

3.7.3 Differences between the two racial groups

Disagreements exist in the literature with regards to the differences in TEWL, skin hydration and skin surface pH when comparing African subjects with Caucasian subjects.

It can be seen from Figure 1 (a) that there was no statistical significant difference between these two racial groups when evaluating TEWL for the mid-forearm for both the barrier creams. Figure 1 (b) however, illustrated a statistical significant difference between Africans when compared to the Caucasians when evaluating the TEWL palm for both barrier creams. Berardesca *et al*. (1998) stated that Africans have an increased TEWL when compared to Caucasians without the application of barrier creams. Even with the application of barrier creams it is not in accordance with the results found in Figure 1 (b). As this significance was only illustrated by the palm values this may be due to the difference between the two measurement sites.

Figure 2 (a) illustrates a statistical significant difference between the two racial groups when evaluating the skin hydration mid-forearm for Reinol Solvgard barrier cream, yet no racial difference was illustrated for Momar Chex. This may suggest that the effect that barrier creams have on the skin barrier function differ. Figure 2 (b) illustrated a statistical significant difference between the two racial groups when evaluating the palm skin hydration (this applied to both barrier creams). Most studies indicated no difference in the skin hydration in African skin when compared to Caucasian skin, yet Treffel *et al*. (1994) indicated a difference between skin hydration that is in accordance with the results found in this research.

Figure 2 (a) illustrates a statistical significant difference between the two racial groups with the skin surface pH (mid-forearm) for the Momar Chex barrier cream, however, no significant differences were found between the two racial groups with skin surface pH mid-forearm for the Reinol Solvgard barrier cream. Figure 2 (b) illustrated no statistical significant difference between the two racial groups with the skin surface pH palm for both the barrier creams. Some studies indicated that Africans have lower skin surface pH than Caucasians, whereas other indicated the opposite effect (Fluhr *et al*., 2008).

3.7.4 Total skin thickness

No statistical significant differences were found with regards to total skin thickness which may be ascribed to the short duration of exposure to the creams which may have prevented any significant changes in the skin to occur which could affect total skin thickness. Please refer to Table 4 on page 73 for tabled values.

3.8 Conclusion

Table 1 represents the category used for this study that describes the effect of the barrier cream on skin surface parameters, whereas Table 2 represents the indication of overall effects of barrier creams studied in this study.

Table 1: Categories indicating positive or negative effect elicited by a barrier cream:

Skin surface Parameter	Increase of parameter values	Decrease in parameter values
TEWL	Negative effect	Positive effect
Skin hydration	Positive effect [4]	Negative effect
Skin surface pH	Negative effect	Positive effect

Note 4: Increases in skin hydration in an excessive form may indicate hyper hydration which may be seen as a negative effect.

Table provides an indication of the overall effects of barrier creams.

Table 2: Effects of barrier creams on skin surface parameters used in the research study:

Barrier Cream	Skin surface Parameters		
	TEWL	Skin hydration	Skin surface pH
Momar Chex	Positive effect	Positive effect	Negative effect
Solvgard	Positive effect	Negative effect	Negative effect

As gathered from Table 7 it can be seen that the Momar Chex barrier cream has more advantages when compared to the Reinol Solvgard barrier cream. Therefore the following the following may be concluded:

- There were short term changes (over a period of 8 hours) or effects on the skin surface parameters after the application of barrier creams.
- Differences were observed between two barrier creams and between the two racial groups.

After thorough investigation and evaluation it may be concluded that the objectives of this research study were reached.

3.9 References:

Agner T, Held E. (2002) Skin protection programmes. Contact Dermatitis; 46: 253-256.

Alvarez MS, Lance BS, Brown H *et al*. (2001) Are barrier creams actually effective? Curr Allergy Asthma Reports; 1: 337-341.

Berardesca E, Pirot E, Singh M *et al*. (1998) Differences in stratum corneum pH gradient when comparing white caucasian and black African-American skin. Br J Dermatol: 139: 855-857.

Berndt U, Wigger-Alberti W, Gabard B *et al*. (2000) Efficacy of a barrier cream and its vehicle as protective measure against occupational irritant contact dermatitis. Contact Dermatitis; 42: 77-80.

Brown T. (2004) Strategies for prevention: occupational contact dermatitis. Occup Med; 54: 450-457.

Courage and Khazaka Electronic GmbH. (2008) Information and operating instructions for Derma Unit SSC3 Sebumeter®/ Corneometer®/ Skin-pH-Meter® and the software for Windows®. Germany:CK

Deflin Technologies Ltd. (2010) User's manual, Wireless Vapometer,. P1-39. Denda M. (2000) Skin barrier function as a self-organizing system. Forma; 15: 227-232.

Drexler H. (2003) Skin protection and percutaneous absorption of chemical hazards. Int Arch Occup Environ Health; 76: 359-361.

Du Plessis J, Stefaniak A, Eloff F *et al*. (2013) International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: Part 2. transepidermal water loss and skin hydration. Skin Res Technol; 19: 265-278.

Fluhr JW, Darlenski R, Berardesca E *et al*. (2008) Ethnic groups and sensitive skin: two examples of special populations in dermatology. Drug Disc Today Disease Mechanisms; 5: 249-263.

Held E, Sveinsdóttir S, Agner T. (1999) Effect of long-term use of moisturiser on skin hydration, barrier function and susceptibility to irritants. Acta Derm Venereol; 79: 49-51.

Kleesz P, Darlenski R, Fluhr JW. (2012) Full-body skin mapping for six biophysical parameters: baseline values at 16 anatomical sites in 125 human subjects. Skin Pharmacol Physiol; 25: 25-33.

Lambers H, Piessens S, Bloem A *et al*. (2006) Natural skin surface pH is on average below 5, which is beneficial for its resident flora. Int J Cosmetic Sci; 28: 359-370.

Madison K. (2003) Barrier function of the skin: “La Raison d’Être” of the epidermis. J Invest Dermatol; 121: 231-241.

Parra JL, Paye M. (2003) EEMCO guidance for the in vivo assessment of skin surface pH. Skin Pharmacol Appl Skin Physiol; 16: 188-202.

Rippke F, Schreiner V, Schwanitz HJ. (2002) The acidic milieu of the horny layer. New findings on the physiology and pathophysiology of skin pH. Am J Clin Dermatol; 4: 261-272.

Schmid MH, Korting HC. (1995) The concept of the acid mantle of the skin: its relevance for the choice of skin cleansers. Dermatol; 191: 276-280.

Schneider T, Cherrie JW, Vermeulen R *et al*. (2000) Dermal exposure assessment. Ann Occup Hyg; 44: 493-499.

Treffel P, Panisset F, Faivre B *et al*. (1994) Hydration, tranepidermal water loss, pH and skin surface parameters: correlations and variations between dominant and non-dominant forearms. Br J Dermatol; 130: 325-328.

Wigger-Alberti W, Caduff L, Burg G *et al*. (1999) Experimentally induced chronic irritant contact dermatitis to evaluate the efficacy of protection creams *in vivo*. J Am Acad Dermatol; 40: 590-596.

Yokota M, Maibach HI. (2006) Moisturiser effect on irritant dermatitis: an overview. Contact Dermatitis; 55: 65-72.

CHAPTER 4: Concluding Chapter

4.1 Summary

Barrier creams are applied to the skin surface, specifically to those areas most frequently exposed to external stressors (Alvarez *et al.*, 2001). Barrier creams are part of a three step process that include 1) skin protection before work, 2) skin cleansing to remove substances from the skin surface and 3) application of skin products after work to repair the skin barrier after damage was sustained and to hydrate the skin surface. Barrier creams form a diffusion barrier against irritants that may otherwise penetrate through the skin surface. One of the concerns of barrier creams is that they are formulated to afford protection against either water-based or oil-based substances, however, one may encounter both of these substances in the working environment (Proksch and Brasch, 2011). Barrier creams are seen as one of the personal protective measures that may be used in the industry. It may be used in conditions or in work situations where it is not practical to wear gloves or where optimal finger mobility is needed (Berardesca *et al*., 1998; Held *et al*., 1999). One cannot, however, compare barrier creams with gloves neither can they replace the function of gloves. Barrier creams were included in this research study to evaluate the effects that they elicit on the skin barrier function through assessment of skin surface parameters. Skin surface parameters have been used in the working environment and laboratory setting to evaluate the skin barrier function. The skin surface parameters included TEWL, skin hydration and skin surface pH. Skin thickness is normally assessed and evaluated as a parameter on its own.

There are several techniques that have been developed to evaluate the actual effect that barrier creams have on the skin barrier function. These studies have however, only been conducted in laboratory settings and few studies have been conducted on barrier creams in the actual working environment (Proksch and Brasch, 2011). The laboratory setting was used as an optimal environment in this study to obtain accurate values as several factors were closely regulated and eliminated. These values may be used as a possible guideline in the work environment during the selection process of barrier creams.

There are interracial variations in skin surface values measured and there are several different racial groups working at a particular work area (Fluhr *et al*, 2008). These variations may explain several tendencies that were indicated in this research.

It was the objectives of the study to compare (a) the short-term effects that selected barrier creams have on skin barrier function and skin thickness of African skin in comparison with Caucasian skin, (b) to compare Momar Chex barrier cream and Reinol Solvgard barrier cream with one another using identical skin parameters (TEWL, skin hydration, skin surface pH and total skin thickness) and (c) to determine how different skin surface parameters are affected over a total time period of 8 hours for both barrier creams. After thorough evaluation it can be concluded that:

(a) Short–term changes were observed in the effect that barrier creams have on barrier function when comparing African participants with Caucasian participants, (b) barrier creams were compared with one another by making use of skin surface parameters and lastly (c) increases and or decreases were observed in skin surface parameters after a period of 8 hours that determined how skin surface parameters were affected. Therefore, the objectives of this study were reached.

Short-term effects of barrier creams on skin surface parameters over a period of 8 hours.

Hypothesis 1:
The application of barrier creams will have a general positive effect on skin barrier function parameters over the short term. General positive effects may be categorised upon a barrier cream that lowers TEWL and skin surface pH and increases skin hydration.

A decrease in TEWL was observed for both barrier creams after 8 hours, racial groups and anatomical sites which was the desired effect. Reinol Solvgard decreased the skin hydration for both racial groups and for both anatomical areas, while Momar chex increased the skin hydration for both racial groups and both anatomical areas. An increase in skin hydration was the desired effect, however, the Reinol Solvgard barrier cream had the opposite effect. Both barrier creams increased the skin surface pH for both racial groups and both anatomical areas, however, the desired effect would have been a more acidic skin surface pH.

The first hypothesis is therefore, partially accepted, as negative effects of the barrier creams on the skin barrier function also occurred.

Hypothesis 2:
The difference in effect of two different brands of water based (oil repellent) barrier creams on skin barrier function will not be statistically significant.

There was no significant difference between the barrier creams for TEWL for both racial groups and anatomical areas. There was a statistical significant difference between the two barrier creams for skin hydration for both racial groups and both anatomical areas. There was a statistical significant difference between the two barrier creams for skin surface pH for Africans for both anatomical areas, yet there was no significant difference between barrier creams for skin surface pH for Caucasians for both anatomical areas.

The second hypothesis is therefore, only partially accepted as there were both significant as well as insignificant differences elicited by the short term use of two different brands of barrier creams.

Hypothesis 3:
A statistical significant difference will exist between the effect elicited from the application of barrier creams over the short term on African versus Caucasian skin.

There was a statistical significant difference between the two racial groups for TEWL for the palm, yet no statistical significant difference was found between the racial groups for TEWL for the mid-forearm. There was a statistical significant difference between the two racial groups for skin hydration for the Reinol Solvgard barrier cream, yet no difference was found between the two racial groups for the Momar Chex barrier cream for the palm. There was a statistical significant difference between the two racial groups for the skin hydration for both barrier creams for the palm. There was a statistical significant difference between the two racial groups for skin surface pH for the Momar Chex barrier cream for the mid-forearm, yet no difference was found between the two barrier creams for Reinol Solvgard for the mid-forearm. No significant difference was found between the two racial groups for skin surface pH for both barrier creams for the palm.

Hypothesis three is therefore, only partially accepted as there were both significant and insignificant differences observed between African versus Caucasian participants.

4.2 Recommendations

4.2 1 Recommendations for future laboratory studies

- Ensure that all the possible factors that may influence the values are eliminated or closely regulated which include extrinsic, intrinsic and experimental factors.
- Ensure that the participants understand, adhere and comply with the requirements of the research.
- Ensure that the instruments are used according to the manufacturers instructions.
- Measurement techniques need to remain constant throughout the entire research study.
- Reinol Solvgard may be tested in combination with a moisturiser to determine if the moisturise hydrates the stratum corneum layer of the skin after the use of the barrier cream.

4.2.2 Recommendations for the use of barrier creams

- Barrier creams should be used according to the substances that they afford protection against.
- Barrier creams should be re-applied every 4 hours (according to specifications from suppliers) and not just once. Barrier creams should be re-applied after every time the employees wash their hands.
- Workers should be educated and informed with regards to the use and application and limitations of the barrier creams.
- Barrier creams should not be used in addition to gloves as they may elicit detrimental effects.
- Reinol Solvgard should be used in combination with a moisturiser at the end of an 8 hour work day shift to hydrate (moisturise) the stratum corneum layer. Moisturisers are used / given to workers in order to hydrate the skin surface as daily work activities may dehydrate it.

4.3 Limitations

- Barrier creams in this study were only tested over a short-term period. There may, however, be different results if these barrier creams are tested over the long term period (weeks or months).

- Literature studies available on the topic of barrier creams are limited and controversial making it difficult to recommend barrier creams to be tested in the laboratory setting and to be used in the working environment.
- Based on the information received from industry it is clear that there is a lack of knowledge in the industry concerning barrier creams as some industries made use of normal moisturisers as opposed to barrier creams.
- No regulatory body exists who can regulate the quality of barrier creams available to the industry to approve barrier creams to be used in the industry.

4.3.1 General challenges with barrier creams

- Some barrier creams afford protection to one type of substance, either oil-based or water-based substances. It is, however, clear that a worker may be exposed to more than one type of substance in any particular work setting.
- In general it may be difficult to enforce personal protective equipment (PPE) and in this instance the worker needs to be well educated on the limitations and uses of the barrier creams.
- Some of the participants were hesitant when one applied the Solvgard barrier cream due to its whitening appearance after it was applied to the skin surface. This problem may exist in the work setting as well, which makes it difficult to implement this type of exposure control. A stigma regarding barrier creams may be created amongst workers making it a difficult task to implement this type of PPE.
- Both barrier creams tested in this research are of a water based nature, however, elicited different effects on the skin barrier function when evaluating skin surface parameters which may be attributed to different ingredients. This makes it difficult to recommend barrier creams of the same type as effects elicited on the skin barrier function are unclear (if not tested).

4.3.2 Barrier creams: The working environment

- The results were obtained in a laboratory setting and several factors were taken into consideration and eliminated which could have influenced the skin surface parameters. It should be noted that not all of these factors can be eliminated in a work setting. The data gathered and presented from this research study are of great value as it may be used as a guideline for the working environment during the selection of one of these two barrier creams that were used in this research.

- The following describes possible problems when one would evaluate these barrier creams in any work setting:
    - It would not be practicable to ensure that all the workers do not smoke.
    - Both male and female are encountered in the working sector.
    - Age was one of the internal factors that was controlled in this research. In the working environment one can encounter different aged groups, which may influence values.
    - It would not be practicable to measure every two hours as it would interfere with a production line in any industry.
    - Employees may wash hands before and after lunch and for personal hygiene purposes that may influence skin surface parameters.
    - Different racial groups are in a work setting.
    - It is not reasonably practicable for employees to acclimatise before each of the measurements as time may be a limiting factor. Therefore, perspiration in hot working environments would have a major impact on TEWL values.

4.4 References:

Alvarez MS, Lance BS, Brown H *et al*. (2001) Are barrier creams actually effective? Curr Allergy Asthma Reports; 1: 337-341.

Berardesca E, Pirot E, Singh M *et al*. (1998) Differences in stratum corneum pH gradient when comparing white caucasian and black African-American skin. Br J Dermatol: 139: 855-857.

Fluhr JW, Darlenski R, Berardesca E *et al*. (2008) Ethnic groups and sensitive skin: two examples of special populations in dermatology. Drug Disc Today Disease Mechanisms; 5: 249-263.

Held E, Sveinsdóttir S, Agner T *et al*. (1999) Effect of long-term use of moisturiser on skin hydration, barrier function and susceptibility to irritants. Acta Derm Venereol; 79: 49-51.

Proksch E, Brasch J. (2011) Contact Dermatitis. *In* Proksch E, Brash J, *eds*. Role of the permeability barrier in contact dermatitis. Springer. P. 121-135. ISBN. 987 3 642 03826 6.

CHAPTER 5: Appendix

5.1 Appendix

5.1.1 Table

Independent t-tests were performed for each of the skin surface parameters at each of the time intervals (0, 2, 4, 6 and 8 hours). Table 8 illustrates the mean and *p*-value for each of the skin surface parameters at the specific time interval.

5.1.2 Informed consent form

An informed consent is attached in the appendix. This informed consent form explains the aim and the procedure of the study, the instruments used and the possible risks of the study. This informed consent form was given to each of the participants that participated in this research study. The research study and the requirements of this research were explained to each of the participants. By signing the informed consent form the participants acknowledged that they understood the procedure and would adhere to the prescribed requirements.

Table 3: Indicates *p*-values for different groups and at a specific time interval

Skin surface parameters	Barrier creams						Racial groups	
	Caucasian (n=21)			African (n=21)			Solvgard (Caucasian versus African)	Momar chex (Caucasian versus African)
	Solvgard (Mean)	Momar Chex (Mean)	*P* value	Solvgard (Mean)	Momar chex (Mean)	*P* value	*P* Value	*P* Value
TEWL MF 0	35.76	34.84	0.75	33.38	36.99	0.12	0.39	0.40
TEWL P 0	463.09	510.30	0.43	306.83	326.00	0.56	**≤ 0.05***	**≤ 0.05***
TEWL MF 2	30.45	32.84	0.42	27.66	31.26	0.18	0.35	0.55
TEWL P 2	435.76	397.14	0.54	191.05	243.19	0.19	**≤ 0.05***	**≤ 0.05***
TEWL MF 4	27.62	32.87	0.05	30.73	32.71	0.54	0.35	0.95
TEWL P 4	418.85	451.72	0.53	239.97	283.15	0.31	**≤ 0.05***	**≤ 0.05***
TEWL MF 6	29.42	32.78	0.20	30.02	33.67	0.17	0.834	0.70
TEWL P 6	435.58	468.15	0.58	274.87	351.77	0.15	**≤ 0.05***	**≤ 0.05***
TEWL MF 8	29.65	34.18	0.18	31.07	30.80	0.93	0.70	0.24
TEWL P 8	428.50	449.09	0.73	264.12	300.76	0.46	**≤ 0.05***	**≤ 0.05***
Skin hydration MF 0	30.45	32.01	0.44	38.52	35.46	0.27	**≤ 0.05***	0.15
Skin hydration P 0	33.34	29.53	0.39	18.87	15.90	0.28	**≤ 0.05***	**≤ 0.05***
Skin hydration MF 2	19.96	50.67	**≤ 0.05***	28.51	48.92	**≤ 0.05***	**≤ 0.05***	0.54
Skin hydration P 2	20.83	40.64	**≤ 0.05***	13.53	19.01	**≤ 0.05***	**≤ 0.05***	**≤ 0.05***
Skin hydration MF 4	15.68	51.78	**≤ 0.05***	22.13	50.40	**≤ 0.05***	**≤ 0.05***	0.62
Skin hydration P 4	18.72	41.70	**≤ 0.05***	12.09	19.71	**≤ 0.05***	**≤ 0.05***	**≤ 0.05***
Skin hydration MF 6	14.23	53.01	**≤ 0.05***	20.26	50.98	**≤ 0.05***	**≤ 0.05***	0.40
Skin hydration P 6	19.12	41.47	**≤ 0.05***	12.65	23.07	**≤ 0.05***	**≤ 0.05***	**≤ 0.05***
Skin hydration MF 8	13.78	53.20	**≤ 0.05***	19.79	51.60	**≤ 0.05***	**≤ 0.05***	0.51
Skin hydration P 8	16.45	42.87	**≤ 0.05***	14.56	23.99	**≤ 0.05***	0.40	**≤ 0.05***
Skin surface pH MF 0	5.38	5.35	0.85	5.47	4.96	**≤ 0.05***	0.61	**≤ 0.05***
Skin surface pH P 0	5.34	5.26	0.46	5.42	5.24	0.28	0.56	0.86
Skin surface pH MF 2	6.23	6.54	0.22	6.24	6.89	**≤ 0.05***	0.97	0.12
Skin surface pH P 2	6.65	6.57	0.65	6.43	6.70	0.05	0.11	0.44
Skin surface pH MF 4	6.42	6.83	0.09	6.38	6.85	**≤ 0.05***	0.84	0.92
Skin surface pH P 4	6.68	6.70	0.89	6.40	6.88	**≤ 0.05***	**≤ 0.05***	0.33
Skin surface pH MF 6	6.35	6.99	**≤ 0.05***	6.47	7.19	**≤ 0.05***	0.58	0.32
Skin surface pH P 6	6.56	6.85	0.06	6.53	6.98	**≤ 0.05***	0.83	0.43
Skin surface pH MF 8	6.40	7.00	**≤ 0.05***	6.40	7.39	**≤ 0.05***	0.96	**≤ 0.05***
Skin surface pH P 8	6.60	6.82	0.20	6.58	7.05	**≤ 0.05***	0.83	0.21

P = Palm MF = Mid-forearm * = Indicates a statistical significant difference

Note: 0, 2, 4, 6 and 8 in Table refers to the specific time interval (in hours) on which each parameter was measured.

Table 4: Indicates mean- and *p*-values for total skin thickness (for the mid-forearm and palm of the hand).

Total skin thickness (Mid-forearm)			
Reinol Solvgard	Mean value (0 hour)	Mean value (after 8 hours)	*p*-value
Caucasian	1.39 mm	1.47 mm	0.78
African	1.31 mm	1.46 mm	
Momar Chex	Mean value (8 hour)	Mean value (after 8 hours)	*p*-value
Caucasian	1.36 mm	1.33 mm	0.55
African	1.37 mm	1.45 mm	
Total skin thickness (Palm)			
Reinol Solvgard	Mean value (0 hour)	Mean value (after 8 hours)	*p*-value
Caucasian	1.58 mm	1.73 mm	0.53
African	1.68 mm	1.83 mm	
Momar Chex	Mean value (0 hour)	Mean value (after 8 hours)	*p*-value
Caucasian	1.62 mm	1.63 mm	0.43
African	1.72 mm	1.73 mm	

NORTH-WEST UNIVERSITY
YUNIBESITI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT
POTCHEFSTROOM CAMPUS

Informed consent: Occupational Hygiene M.Sc study 2013

Purpose: Several parameters are used to evaluate the integrity of the skin barrier function and include, TEWL (transepidermal water loss), skin hydration, skin surface pH and skin thickness. The purpose of this study is to evaluate the effect that different barrier creams have on the skin barrier function by measuring the parameters of the skin surface. The measurement related factors include measurement on different anatomical areas, different barrier creams used, different time intervals and different ethnic groups.

Procedure: Baseline values of TEWL, skin hydration, skin surface pH and total skin thickness will be measured. TEWL will be measured using a closed chamber Vapometer. Skin hydration will be measured using a Corneometer 825 and the skin surface pH using a pH meter (pH905). Total skin thickness will be measured by making use of the Ultrascan UC22 - TBS0061B. After baseline values are measured the barrier creams will be applied to the experimental arm and the skin surface parameters will be measured every 2, 4, 6 and 8 hours. Barrier creams will be re-applied every 2, 4 and 6 hours after the parameters have been measured. This research will take place over a period of two days as there are two barrier creams that need to be evaluated.

Risks: All measurements are non-invasive and the above mentioned probes as well as the Ultrascan machine will be placed on the skin surface for approximately 1-15 seconds during each measurement. One may have an allergic reaction towards the barrier cream. If any signs of it is seen participant will be excluded from study.

All personal information regarding study participants will be kept confidential and all data will be kept confidential and all data will be reported anonymously.

This study will be carried out under the ethical number NWU-00097-10-55 given by the NWU Ethics Committee.

Informed consent

I hereby agree to participate in this research for a period of two days. However, I understand that I am free to leave at any time during the study if I so desire. I, furthermore, understand the measurement procedure and my role in it and that there are no direct risks involved in taking part in this research study.

I will not consume any alcohol or caffeine for 12 hours before this session at in can influence the results of this study.

I will not use any soaps or moisturisers on my hands or arms 12 hours before the session.

I will not bath nor shower on the day of the study.

I (full names and surname) _____ understand the above mentioned facts and procedures.

_____

Signature of participant

_____

Signature of researcher

_____

Date