COLORIMETER

How accurate is the use of colorimeters to grade erythema on melanin-rich skin compared to the subjective clinical method used today?

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ABSTRACT

This literature review evaluates the accuracy of colorimeters in grading erythema on melanin-rich skin compared to subjective clinical methods. There is an increasing diversity in Norwegian society and thus the need for equality in dermatological treatment arises. The research investigates whether current clinical practices in erythema grading, which are significant for treatment decisions, are equally effective for all skin tones. By assessing various methods for erythema measurement, this study aims to identify potential improvements in dermatological care for individuals with melanin-rich skin, thus addressing a gap in equality in medical treatment.

The method entails a systematic analysis of recent articles utilising colorimetry or spectrophotometry in their methodology. The end result is gaining an understanding of the efficacy and limitations of colorimetry across a range of skin tones, providing insight and potential standardisation in clinical practice.

Results demonstrate that colorimeters and spectrophotometers effectively capture detailed colour compositions of the skin regardless of pigmentation levels. However, challenges are seen within detecting subtle changes in erythema for darker skin tones. Additionally, questions arise regarding the potential influence of the lightness factor (*L) has on erythema, which in turn could lead to potential interpretation errors of erythema.

In conclusion, none of the articles provided satisfactory results to fully answer the research question. Some articles suggest that colorimetry may be a more reliable method than visual assessment, but the degree of accuracy remains uncertain based on their results. Further research is needed to address this question thoroughly, therefore I propose a protocol for future research in an attempt to directly answer the question at hand.

INTRODUCTION

In recent years there has been an increasing awareness of diversity within the dermatological field. There have been several articles published, from fellow medical students as well as professors in the field criticising our narrow minded approach to dermatology (1–4). Norwegian society is becoming increasingly diverse, with people from all ethnicities and cultures, yet in medical school we barely learn about how different diseases look on melanin-rich skin. These articles, and through my own experience through my university degree, made me start to question the equality between ethnicity and dermatological treatment.

It is known that people with darker skin tones do suffer from psoriasis, eczema and many other skin conditions, yet many of the grading systems to evaluate severity of disease are based on Caucasian disease patterns. Scoring systems such as Psoriasis Area and Severity Index (PASI) and Eczema Area and Severity Index (EASI) base their score on visual qualities, such as erythema, thickness and scaling of the skin. It is clear that observing erythema in melanin-rich skin, compared to lighter skin, can be challenging, especially if the clinician does not have enough experience with darker skin tones. However, as the clinical practice in Norway is today, erythema grading is key to assess the severity of a skin disease. According to the Norwegian guidelines (September 2021) the threshold for receiving biological treatment against psoriasis is PASI > 10 and DLQI > 10 (5). This means the grading of erythema plays a big role in who receives this type of treatment. This leads me to the overall question; do people of colour receive less treatment possibilities for skin disorders than Caucasians?

The area of focus I chose to embark on, was the measure of erythema. Partly because I saw this as an area of big potential to close the gap of inequality, and partly due to the fact that

Rikshospitalet had acquired a colorimeter. How does one go about scoring erythema in an objective way? How does one reduce the variables in the scoring method to allow for more reliable results? How accurate is an alternative measure of erythema on melanin-rich skin compared to the subjective clinical method used today? These were all questions I wanted to explore.

I will do an in depth study on the aspects of erythema on melanin-rich skin, by looking at articles that use alternate methods for determining skin colour and change in skin colour on a range of skin types. I want to compare these methods to the clinical practice in use today. The goal is to explore an alternate clinical practice that could allow for equality within dermatology across all ethnicities. Allowing patients the correct treatment, without their skin pigmentation being a limiting factor.

This review is meant to add to the ongoing debates and awareness campaigns, and shed light on the use of technology to close the gap of treatment options between darker skin and lighter skin. It is also meant as an article to present data on the efficacy of colorimetry and urge Rikshospitalet to standardise their clinical practice, and be an example to others to embrace innovation and new thinking also within their dermatological department, bringing about more equality across all skin tones.

THEORY

Anatomy of the Skin

The skin is the outer organ of our body. It is divided into 3 layers, epidermis, dermis and subcutis.

Epidermis

The epidermis, serving as the outermost epithelial layer of the skin, acts as a vital protective barrier for the body. Its primary functions include preventing water loss and safeguarding against the entry of foreign particles and organisms. The epidermis is made up of keratinised stratified squamous epithelium, composed of four key types of cells: keratinocytes (responsible for skin

formation), melanocytes (cells that produce pigments), Langerhans cells (immune cells), and Merkel cells (6).

Keratinocytes

Keratinocytes, the primary skin cells responsible for forming the squamous epithelial structure of the epidermis, undergo differentiation and maturation from the basal layer to the surface. During this process, they accumulate keratin as they move towards the outermost layer. The epidermis is organised into four distinct layers from the deepest to the most superficial: stratum basale, stratum spinulosum, stratum granulosum, and stratum corneum.

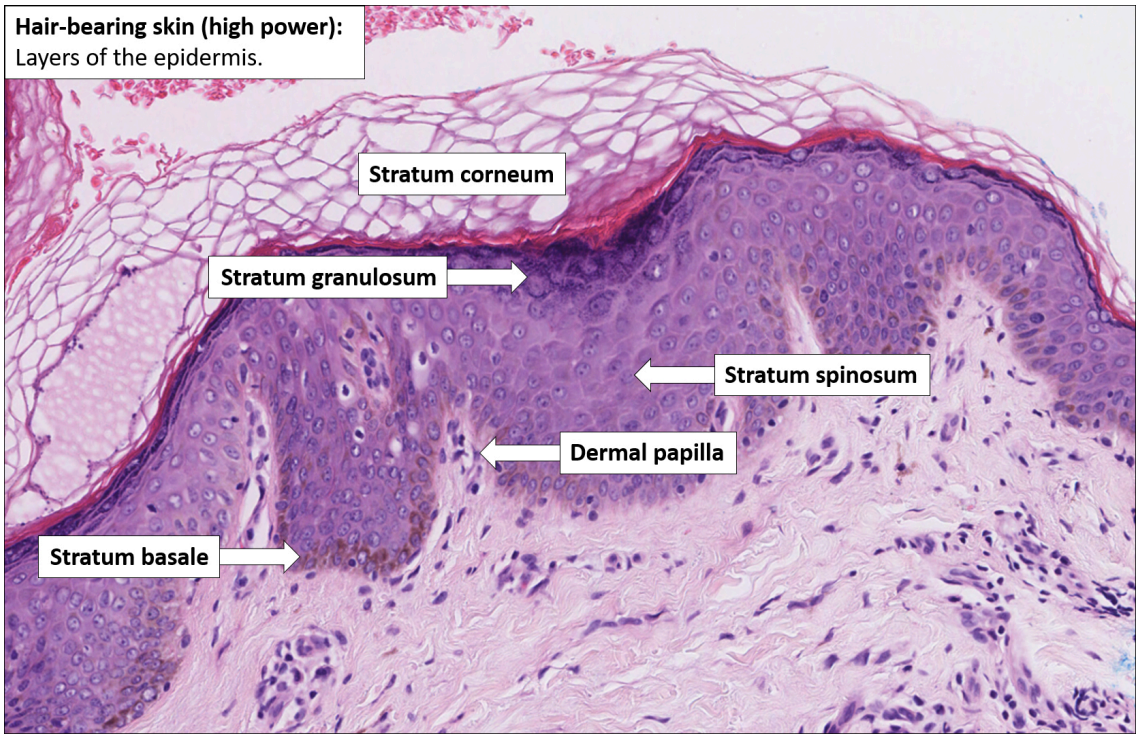

Figure 1. Histological image of the anatomical layers in the epidermis.(7)

Below the stratum basale lies the basal membrane, marking the boundary between the epidermis and the dermis.

The epidermis also gives rise to specialised adnexal structures, such as hair follicles, which are direct extensions of the epidermis folding into the underlying dermis. The presence of adnexal

structures varies across different areas of the body, reflecting the specific functions of each skin region (6).

Melanocytes

These are cells found in the stratum basale of the epidermis. Melanocytes produce melanin, a pigment responsible for the various colours observed in the skin. Once melanin is synthesised, it is packaged into structures known as melanosomes. Subsequently, these melanosomes are transferred to the keratinocytes, where they are placed superiorly to the nuclei of the keratinocytes. These serve as a protective mechanism against incoming ultraviolet radiation (6).

Melanin

Melanin exists in three forms within the human body: eumelanin, pheomelanin, and neuromelanin. Melanocytes in the epidermis produce both eumelanin, responsible for the brown-black colour of the skin, and pheomelanin, contributing to the yellow-red coloration.

UV radiation primarily stimulates melanogenesis, leading to an increased production of eumelanin. Skin pigmentation results from the accumulation of melanin-containing melanosomes in the stratum basale of the epidermis. The diversity in skin pigmentation arises from variations in the number of melanosomes in keratinocytes and the proportions between eumelanin and pheomelanin. The overall melanin density correlates with the darkness of the skin.

Eumelanin, besides providing colour, acts as a UV-absorbing compound, antioxidant, and free radical scavenger. Populations closer to the equator, exposed to higher UV levels, tend to have a larger proportion of eumelanin, reflecting an evolutionary adaptation. Conversely, populations farther from the equator possess a higher proportion of pheomelanin, crucial for cutaneous vitamin D production in response to UV light exposure, representing an evolutionary response to reduced UV light availability (8).

Langerhans Celler

Langerhans cells, immune cells in the epidermis, detect and break down allergens. After breaking them down, they migrate to the dermis and continue into the lymphatic system where

they present the allergens to lymphocytes in lymph nodes. This triggers an immune response and establishes a memory for future encounters (6).

Dermis

The dermis, a connective tissue layer of the skin, provides structural support through collagen and elastin fibres. It houses various components, including nerves, blood vessels, epidermal adnexal structures, and cells such as mast cells, vascular smooth muscle cells, specialised muscle cells, and fibroblasts. Mast cells release histamine and other substances when disturbed, while fibroblasts contribute to collagen fibre production and play a role in dermal repair processes (6).

Subcutis

Subcutis is the fat layer below the dermis. This layer mainly contains adipocytes, nerves and blood vessels (6).

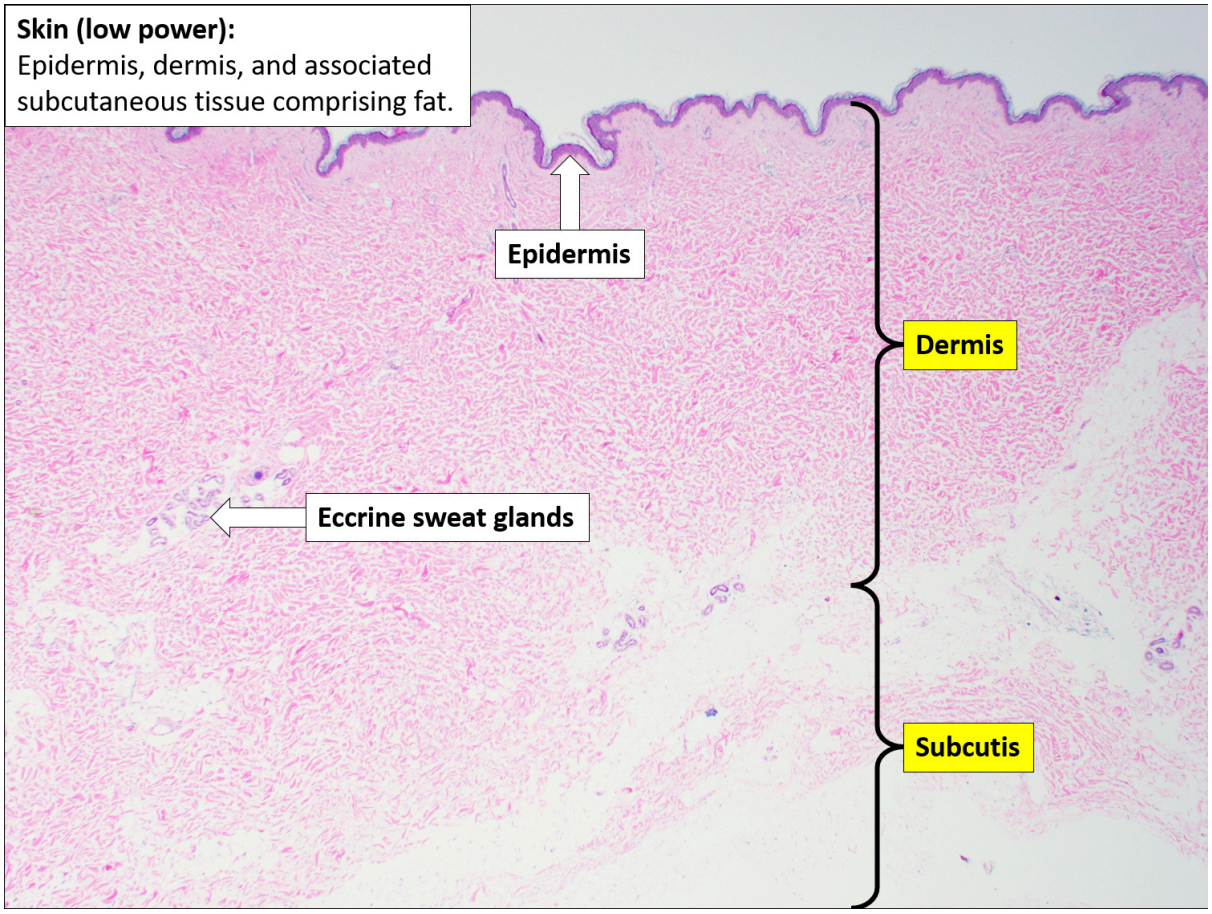

Figure 2. Histological image of the anatomical layers of the skin.(7)

Fitzpatrick Skin Phototype

The Fitzpatrick skin phototype classification, established by Thomas B. Fitzpatrick in 1975, describes how skin responds to UV light based on melanin pigment. This reaction is assessed through the skin's tanning ability. Pale skin burns easily and tans slowly, therefore needing more protection against sun exposure. Darker skin burns less and tans more easily, however is more prone to develop postinflammatory pigmentation after injury (9).

Skin types are graded I-IV for Caucasians, with later additions of types V and VI for dark-skinned individuals. However, these additions are not based on tanning and burning but rather on pigmentation and ethnic origin (9). The classification remains constant throughout a person's life, reflecting their innate characteristics. While individuals with photosensitivity may burn easily due to certain conditions or medications, their tanning ability remains unaffected.

Table 1. Fitzpatrick classification system.(10)

Skin type	**Typical Features**	**Tanning Ability**
I	Pale white skin, blue/green eyes, blond/red hair	Always burns, does not tan
II	Fair skin, blue eyes	Burns easily, tans poorly
III	Darker white skin	Tans after initial burn
IV	Light brown skin	Burns minimally, tans easily
V	Brown skin	Rarely burns, tans darkly easily

Skin type	Typical Features	Tanning Ability
I	Pale white skin, blue/green eyes, blond/red hair	Always burns, does not tan
VI	Dark brown or black skin	Never burns, always tans darkly

Widely used in dermatology, the Fitzpatrick system aids in analysing sun sensitivity, estimating UV, PUVA, and laser treatment doses, and serves as a self-assessment tool. The associated questionnaire evaluates genetic constitution, UV-light reaction, and tanning habits, assigning a final score corresponding to the Fitzpatrick skin type (10,11).

Table 2. Fitzpatrick self evaluation form.(12)

Genetic					
	Score				
Characteristics	0	1	2	3	4
Eye colour	Light blue, green, grey	Blue, green, grey	Dark blue, green, hazel	Dark brown	Brown/black
Natural hair colour	Red	Blonde	Brown	Dark brown	Black
Skin colour (unexposed area)	Pink	Pale	Light brown or olive	Brown	Dark brown
Freckles on unexposed areas	Many	Several	Few	Rare	None
Sensitivity					
	Score				

Exposure	0	1	2	3	4
Skin reaction when exposed to the sun for extended periods of time	Severe burns, blistering, peeling	Moderate burns, blistering, peeling	Burns sometimes followed by peeling	Burns rarely	No burns
Tanning after sun exposure	Never	Rarely	Sometimes	Often	Always
Grade of tanning	Not at all	Light tan	Medium tan	Dark tan	Very dark tan
Face sensitivity to sun exposure	Very sensitive	Sensitive	Mildly sensitive	Resistant	Very resistant
<u>Tanning habits</u>					
	Score				
Exposure	0	1	2	3	4
Frequency of tanning	Never	Rarely	Sometimes	Often	Always
Time of last tanning	> 3 months ago	Last 2-3 months	Last 1-2 months	Last week	Last day

Table 3. Fitzpatrick self evaluation form scoring.(12)

Fitzpatrick skin type	**Skin type score**
0-7	I
8-16	II
17-25	III
25-30	IV
>30	V-VI

Erythema

Erythema, characterised by redness resulting from skin injury or inflammation, is rooted in the pathophysiology of arteriole dilation. The heightened blood flow in the superficial blood vessel network imparts a visible reddish hue to the skin's surface. This is due to the presence of haemoglobin in the blood. Detection of this redness becomes challenging in melanin-rich skin, where the melanin conceals the red colour. Clinically, erythema serves as a criteria for gauging the severity of various diseases and skin irritants (13).

PASI and EASI

The Psoriasis Area of Severity Index (PASI) serves as a scoring system for evaluating the severity of psoriasis. This assessment involves selecting a psoriatic skin area and determining the intensity of redness, thickness, and scaling, assigning scores ranging from 0 to 4 in each category. 0 meaning none, 1 is mild, 2 is moderate, 3 is severe and 4 is very severe. Additionally, the affected body area is assessed in four regions: head and neck, upper limbs, trunk, and lower limbs. The percentage of affected skin in each region is given a score. Once the intensity score and the area affected with psoriasis is determined, numbers for each region are multiplied with each other and added up to give the total PASI score. View table 4 below for more detailed explanation of the calculations (14).

The Eczema Area and Severity Index (EASI) is similar to PASI but is tailored for assessing patients with eczema. The EASI severity score involves totaling the intensity scores for four signs: redness, thickness, excoriation, and lichenification. The overall EASI score is then calculated in a manner similar to the PASI score (15).

PASI Calculation

Table 4. PASI calculations to determine complete PASI score.

PASI CALCULATION: HEAD & NECK				
Intensity (A1)	**Score**	**Surface Area (C1)**	**Score**	Add each value to get the total intensity for this body part:

Erythema (a)	0-4	0%	0	a + b + c = A1 Multiply A1 with area constant: A1 x 0,1 = B1 Surface area score calculation: B1 x C1 = D1 Total formula for surface area PASI score head and neck: D1 = (a + b + c) x 0,1 x C1
Thickness (b)	0-4	1-9%	1	
Scaling (c)	0-4	10-29%	2	
Area constant for head and neck = 0,1		30-49%	3	
		50-69%	4	
		70-89%	5	
		90-100%	6	
PASI CALCULATION: UPPER LIMBS				
Intensity (A2)	**Score**	**Surface Area (C2)**	**Score**	Add each value to get the total intensity for this body part: a + b + c = A2 Multiply A1 with area constant: A2 x 0,2 = B2 Surface area score calculation: B2 x C2 = D2 Total formula for surface area PASI score upper limbs: D2 = (a + b + c) x 0,2 x C2
Erythema (a)	0-4	0%	0	
Thickness (b)	0-4	1-9%	1	
Scaling (c)	0-4	10-29%	2	
Area constant for upper limbs = 0,2		30-49%	3	
		50-69%	4	
		70-89%	5	
		90-100%	6	
PASI CALCULATION: TRUNK				
Intensity (A3)	**Score**	**Surface Area (C3)**	**Score**	Add each value to get the total intensity for this body part:

<table>
<tr><td>Erythema (a)</td><td>0-4</td><td>0%</td><td>0</td><td rowspan="7">a + b + c = A3

<u>Multiply A1 with area constant:</u>
A3 x 0,3 = B3

<u>Surface area score calculation:</u>
B3 x C3 = D3

<u>Total formula for surface area PASI score trunk:</u>
D3 = (a + b + c) x 0,3 x C3</td></tr>
<tr><td>Thickness (b)</td><td>0-4</td><td>1-9%</td><td>1</td></tr>
<tr><td>Scaling (c)</td><td>0-4</td><td>10-29%</td><td>2</td></tr>
<tr><td colspan="2" rowspan="4">Area constant for trunk = 0,3</td><td>30-49%</td><td>3</td></tr>
<tr><td>50-69%</td><td>4</td></tr>
<tr><td>70-89%</td><td>5</td></tr>
<tr><td>90-100%</td><td>6</td></tr>
<tr><td colspan="5">PASI CALCULATION: LOWER LIMBS</td></tr>
<tr><td>Intensity (A4)</td><td>Score</td><td>Surface Area (C4)</td><td>Score</td><td rowspan="7"><u>Add each value to get the total intensity for this body part:</u>
a + b + c = A4

<u>Multiply A1 with area constant:</u>
A4 x 0,4 = B4

<u>Surface area score calculation:</u>
B4 x C4 = D4

<u>Total formula for surface area PASI score lower limbs:</u>
D4 = (a + b + c) x 0,4 x C4</td></tr>
<tr><td>Erythema (a)</td><td>0-4</td><td>0%</td><td>0</td></tr>
<tr><td>Thickness (b)</td><td>0-4</td><td>1-9%</td><td>1</td></tr>
<tr><td>Scaling (c)</td><td>0-4</td><td>10-29%</td><td>2</td></tr>
<tr><td colspan="2" rowspan="4">Area constant for lower limbs = 0,4</td><td>30-49%</td><td>3</td></tr>
<tr><td>50-69%</td><td>4</td></tr>
<tr><td>70-89%</td><td>5</td></tr>
<tr><td>90-100%</td><td>6</td></tr>
</table>

Complete PASI score = D1 + D2 + D3 + D4

Human Perception of Colour

Colorimetry operates on the principles of determining colour similarly to how the human eyes and brain perceive colour. Our ability to perceive colour is a result of the stimulation of photoreceptor cells in the retina, which send signals to the visual cortex, interpreting these signals into specific colours. Two theories underlie human colour perception: the trichromatic colour theory and the opponent-process theory (9).

The trichromatic colour theory is based on the existence of three types of colour-sensitive photoreceptors, each with a distinct spectral sensitivity range within the visual spectrum—short, medium, and long wavelengths corresponding to blue, green, and red colours (9).

On the other hand, the opponent-process theory pairs certain colours together, such as red and green, blue and yellow, and black and white. These colours are antagonistic, meaning the presence of one colour (wavelength) will inhibit its antagonist (9).

These theories form the foundation for the development of colorimetric instruments, enabling us to compare human perception of colour and colorimetry, as both are grounded in the same underlying principles (9).

Colorimetry

This is the science used to quantify and describe human colour perception. The technique allows for three values (tristimulus values) to be derived. These numbers enable colours to be placed in a three-dimensional colour space, and interpreted in the same way as for a human observer (16).

Colorimeter

A colorimeter serves as a tool for measuring colour objectively, finding applications in both chemical and medical research. Its operational principle is rooted in the trichromatic colour theory, explaining how humans perceive colour (17).

In a medical context, the colorimeter functions by illuminating the skin surface with a xenon lamp. The light is then reflected perpendicular to the skin which is detected by the colorimeter. It analyses the wavelength of the reflected light and assigns a colour based on its wavelength, 450 nm (blue), 560 nm (green), and 600 nm (red). The resulting data is numerically expressed using the L*a*b* colour system (17).

These numerical values can be further utilised in mathematical calculations to precisely determine an individual's skin tone or assess changes in the colour of a specific region (17).

Spectrophotometer

A spectrophotometer is a device employed for colour measurement, often favoured in research for its perceived accuracy compared to a colorimeter. Spectrophotometers can measure the complete spectral range of light between 360 and 700 nm, detecting colour changes that may not be discernible to the human eye (9).

Colorimeters analyse light in the CIELAB colour space, whilst spectrophotometers can analyse with the use CIELAB colour space as well as other colour spaces, giving it a wider range of function (9).

CIE: A Systematic Approach to Color

The Commission Internationale de l'Éclairage (CIE) has developed a systematic approach to interpreting colour based on our eyes' natural capacity to perceive colour. The CIE has defined a standardised light source and, subsequently, the standard observer response function. This process allows the numerical specification of colour through three values known as tristimulus values. These values serve as the foundation for various uniform colour scales, with CIELAB being the most significant among them (16).

CIELAB and cutaneous colorimetry

CIELAB is a 3D colour space consisting of 3 axes that has been developed by the Commission Internationale de l'Éclairage (CIE) to correspond to skin colour. *L is grey scale 0-100

(black-white), corresponding to the level of pigmentation of the skin. *a is the red/green axis and corresponds to erythema. *b is the yellow/blue axis and corresponds to tanning.
The *L, *a and *b can be used to calculate colour change (ΔE) (9).

$$\Delta E^*_{ab} = \left((\Delta L^*)^2 + (\Delta a^*)^2 + \left(\Delta b^* \right)^2 \right)^{\frac{1}{2}}$$

ΔE greater than 1 indicates colour difference observable by the human eye (9).
*L, *a and *b measurements can be plotted into a mathematical equation to calculate the Individual Typology Angle:

$$ITA^o = \arctan\left(\frac{L^* - 50}{b^*}\right) * \frac{180}{\pi}$$

This is an objective classification of skin colour (measured in angles), that is comparative to Fitzpatrick skin phototype (9). ITA is divided into the following categories:

- Very light > 55
- Light 55 - 41
- Intermediate 41 - 28
- Tan 28 - 10
- Brown 10 - -30
- Dark < -30

This objective classification can eliminate the lack of reliability of self reporting and subjective assessment of Fitzpatrick skin phototype (9).

RESEARCH QUESTION

How accurate is the use of a colorimeter to grade erythema on melanin-rich skin compared to the subjective clinical method used today?

METHODOLOGY

Search Strategy

I did a systematic search in the big databases Pubmed, Cochrane Library and Medline. I also selected three specific dermatological journals with the criteria of high impact factor - Journal of the American Academy of Dermatology (Impact factor 13,8) (18), Journal of Investigative Dermatology (Impact factor 7,590) (19), British Journal of Dermatology (Impact factor 10,3) (20).

Keywords I decided to include in my search were:

- "dark skin", "melanin rich", "black skin", "african skin", "indian skin", "pigmented skin", "tan skin", "dark-complexioned".
- "erythema*", "redness", "inflammation", "skin pigmentation", "erythema scale".
- "Colorimeter", "colorimetry", “spectrophotometer”.

I included only English articles and set a time frame of the last 3 years, 2020-2023.
I did not specify the type of article in my search, such as original article or metaanalysis.

On the 2. October 2023 I did the following search in PubMed, Cochrane Library, Medline, Journal of the American Academy of Dermatology, Journal of investigative dermatology and British Journal of dermatology :
("dark skin" OR "melanin rich" OR "black skin" OR "african skin" OR "indian skin" OR "pigmented skin" OR "tan skin" OR "dark-complexioned") AND ("erythema*" OR "redness" OR "inflammation" OR "skin pigmentation" OR "erythema scale") AND ("colorimeter" OR "colorimetry" OR “spectrophotometer”).

The results of my systematic search was: 5 articles in PubMed, 3 articles in Cochrane Library, 5 articles in Medline, 1 article in the Journal of the American Academy of Dermatology, 9 articles in the Journal of investigative dermatology and no results in the British Journal of Dermatology.

After completing the search and removing duplicates I had a total of 18 articles.

Inclusion and Exclusion Criteria

Inclusion criteria was articles including my selected search words, published between January 2020 - October 2023. Articles needed to include colorimeter or spectrophotometer in their methodology and research needed to have been done on live human subjects.

Exclusion criteria excluded articles on the basis of: did not use colorimeter or spectrophotometer in their methodology, colorimeter or spectrophotometer was not used on the surface of human skin. Results that turned out to be registries of ongoing clinical trials were also excluded.

Selection Process

I set up a synthesis matrix for my articles found in my systematic search. After plotting my 18 articles into my synthesis matrix I screened them for my inclusion and exclusion criteria. This screening process left me with 9 articles. After reading the 9 articles I ended up excluding further 1 article on the basis that they did not use the results from the spectrophotometer in any analysis later in their article. Rendering the article not relevant to my research question.

1 article in my search was in fact published in 2019. For it to have been included in my search for articles in the time frame 2020-2023 it must have been revised after publication. I have chosen to include this article in my analysis due to its relevance to my research question.

In the end I had a total of 8 articles, 6 original articles and 2 meta-analyses. Articles are summarised in the table below.

Table 5. Articles included in my study.

Articles included in my study				
Tittle	Author	Type of study	Published	Source
A colorimetric comparison	Kinjiro Amano, Kaida Xiao,	Randomised	2020	(21)

of sunless with natural skin tan	Sophie Wuerger, Georg Meyer	control trial		
Chromometric assessment of drug skin tolerance: A comparative study between Africans and Caucasians skins	Hope T. Sounouvou, Anna Lechanteur, Joëlle Quetin-Leclercq, Géraldine PieL, Anne-Françoise Donneau, Fernand Gbaguidi, Brigitte Evrard	Randomised control trial	2019	(17)
Melanin has a Small Inhibitory Effect on Cutaneous Vitamin D Synthesis: A Comparison of Extreme Phenotypes	Antony R. Young, Kylie A. Morgan, Tak-Wai Ho, Ngozi Ojimba, Graham I. Harrison, Karl P. Lawrence, Nihull Jakharia-Shah, Hans Christian Wulf, J Kennedy Cruickshank and Peter A. Philipsen	Randomised control trial	2020	(22)
Photoprotection of the Skin from Visible Light–Induced Pigmentation: Current Testing Methods and Proposed Harmonisation	Henry W. Lim, Indermeet Kohli, Corinne Granger, Carles Trullas, Jaime Piquero-Casals, Mridvika Narda, Philippe Masson, Jean Krutmann and Thierry Passeron	Meta-analysis	2021	(23)
Quantifying the confounding effect of pigmentation on measured skin tissue optical properties: a comparison of colorimetry with spatial frequency domain imaging	Thinh Phan, Rebecca Rowland, Adrien Ponticorvo, Binh Cong Le, Seyed A. Sharif, Gordon T. Kennedy , Robert H. Wilson and Anthony J. Durkin	Randomised control trial	2022	(24)

Research Techniques Made Simple: Cutaneous Colorimetry: A Reliable Technique for Objective Skin Colour Measurement	Bao Chau K. Ly, Ethan B. Dyer, Jessica L. Feig, Anna L. Chien and Sandra Del Bino	Meta-analysis	2020	(9)
Risk of Migraine in Europeans with Low Melanin Levels —A Population Based Case-Control Study	Magdalena Kobus, Elzbieta Zadzinska, Aneta Sitek, Jacek Pełka, Jacek J. Roznіecki and Bogusław Antoszewski	Case-control study	2022	(25)
Skin type specific photobiological response to visible light is mediated by constitutional melanin	Hester Gail Lim, Michelle L. Kerns, Isabelle D. Brown, Sewon Kang, Anna L. Chien	Randomised control trial	2022	(26)

Systematic Search Flowchart:

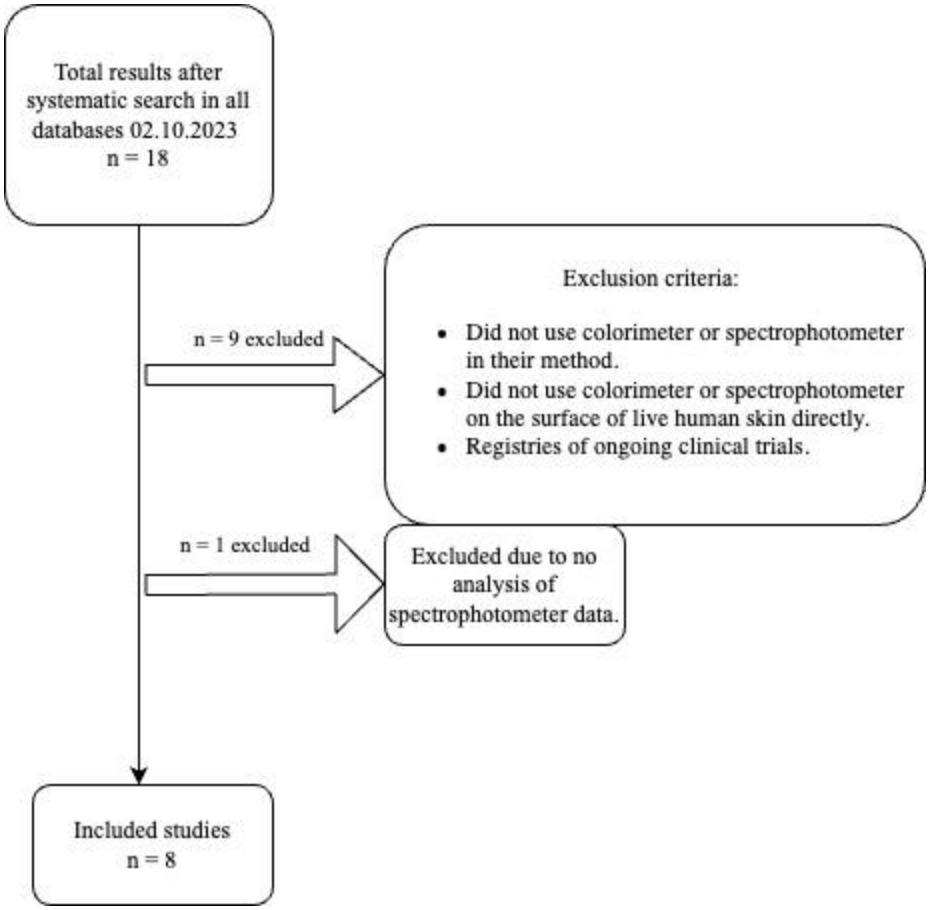

Figure 3. Flowchart illustrating the systematic search methodology for articles.

RESULTS

The articles I reviewed and analysed encompass a diverse range of topics and research questions, united by a common thread—the utilisation of colorimeters or spectrophotometers in their methodologies.

Comparing Methodology

After a comprehensive review of the six original articles obtained through my search, I began to discern certain methodological trends that were relevant to my research question. I specifically honed in on aspects such as sample size, the precise methodology for measuring skin colour, as well as their statistical analysis of the colour measurements. This was what I deemed relevant to support my hypothesis.

The study designs of the six original articles included five randomised control trials and one case-control study. Despite the broad spectrum of dermatological subjects investigated, these studies exhibited similarities in their participant profiles, albeit with some outliers.

Summary of Participants in each Original Article

Table 6. Summary of description of participants in each original article.

SUMMARY OF PARTICIPANTS IN EACH ORIGINAL ARTICLE						
	Article 1 (21)	**Article 2** (17)	**Article 3** (19)	**Article 4** (22)	**Article 5** (25)	**Article 6** (26)
Total number of participants	160	20	120	15	255	16
Divided into test group and control group	Yes	Yes	Yes	No	Yes	No
Number of participants in test group	100	10	67	-	148	-
Number of participants in control group	60	10	35	-	107	-
Number of females	Test group: n=83 Control group: n=46	Test group: n=4 Control group: n=7	Test group: n=46 Control group: n=25	n=6	Test group: n=115 Control group: n=64	n=11
Number of males	Test group: n=17 Control group: n=14	Test group: n=6 Control group: n=3	Test group: n=21 Control group: n=10	n=9	Test group: n=33 Control group: n=43	n=5
Age of participants	Test group: 18-45 Control group: 18-39	Test group: mean age = 34 Control group: mean age = 36	Mean age range across Fitzpatrick skin phototypes: 20-29	20-51	Test group: 19-76 Control group: 21-74	Mean age = 25
Exclusion criteria	Previous used tanning products < 4	Unhealthy.	Exposure to UVR the previous 4	Dermatological complications	Participants declaring sunbathing or	History of photosensitive disorders or

	weeks prior. Pregnant. Acute or chronic disease and dermatological problems.		months. People taking photosensitising medication. Pregnant. Skin conditions or allergies. Organ transplant recipient.		using artificial sources of UV exposure (e.g., sunbeds) within the last 3 months	intake of photosensitising drugs.
Diversity in ethnicity	Test group: 94/100 = caucasian. 6 = non-white. Control group: 60/60 = caucasian	Test group: 10/10 = african Control group: 10/10 = caucasian	Yes, but not specified in ethnicity rather fitzpatrick grade I-VI.	Yes, but not specified which ethnicity.	Yes, but not specified which ethnicities.	Yes, but not specified which ethnicities. Light (ITA >41): n=6 Intermediate (ITA 10-41): n=3 Dark (ITA <10): n=6
Diversity in fitzpatrick skin phototype	No	Yes	Yes	No	Does not specify	No, classifies using ITA.

The six articles encompass a diverse range of total participants, varying from 15 to 255 across their respective studies. Four out of the six articles employed both test and control groups (17,21,22,25), while the remaining two utilised the test group as its own control (24,26). All the studies divided their participants into females and males. With a majority of the studies having an overweight of females, the exception being one article (24). Age distribution showed considerable variability, with all studies restricting participants to those aged 18 and above. The age range spanned from 19 to 76 years in the largest specified range (25) and 20 to 29 years in the smallest (22). However, two articles only provided mean age without specifying the overall range (17,26).

Exclusion criteria were tailored to the specific research questions, and a summarised list is presented in Table 6.

Assessing diversity in ethnicity and Fitzpatrick skin phototype was crucial for evaluating the methodology's applicability across different skin tones. Summarised in table 6, many articles showcased a diverse population. Ethnicity-based divisions, such as African vs. Caucasian (17),

and Fitzpatrick skin phototype categorization from I to VI (22), were observed in some studies. Several articles included participants with varied melanin pigmentation without explicitly detailing the classification method (24,25). One study employed Individual Typology Angle (ITA) to classify participants (26). Notably, only one of the six original articles predominantly featured Caucasian participants, aligning with its research focus that lacked comparisons between ethnicities and skin tones (21).

Summary of Digital Measurements of Skin Colour in each Original Article

Table 7. Summary digital measurement of skin colour in each original article.

SUMMARY OF DIGITAL MEASUREMENT OF SKIN COLOUR IN EACH ORIGINAL ARTICLE						
Article	**Measuring Tool**	**Standardised Conditions**	**Measurement Locations**	**Number of Measurements**	**Timing of Measurements**	**Colour Space**
1 (21)	Spectrophotometer (model CM-700d, KonicaMinolta, Tokyo, Japan)	8 mm aperture and low-pressure mask, Illuminant D65 (standard lighting), CIE 2 degree standard observer, Spectral range 400nm - 700nm in 10nm steps	Inner forearm of both arms.	3 measurements per site	1 day before, 4h and 24h after DHA tanning gel application	CIELAB colour space
2 (17)	Minolta® Chromameter CR-400 driven by the software SpectraMagicTMNX	Placed on the skin surface, avoided pressure	Three sites on the anterior forearm	4 measurements per site	Before and after cream removal	CIELAB colour space
3 (22)	Konica Minolta Spectrophotometer CM-700d, Chroma Meter CR-400, Konica Minolta Sensing, Inc., Tokyo	Instrument gently placed vertically on the skin, with excess pressure avoided (no other forms of standardisation specified)	Three sites on the buttocks	3 measurements per site	One time	CIELAB colour space

4 (24)	Chroma Meter CR-400, Konica Minolta Sensing, Inc., Tokyo Reflect RS® (Modulim, Inc., Irvine, California)	No specifications	Three sites on right outer forearm	Not specified	Not specified	CIELAB colour space
5 (25)	CR-400, KonicaMinolta	No specifications	Inner forearms and buttocks	3 measurements per site	One time	CIELAB colour space, RGB colour model
6 (26)	Not specified	Dermospectrophotometer calibrated before every use	Inner forearms and buttocks	Not specified	Before and after irradiation	CIELAB colour space

Comparing the methodologies employed to measure skin colour or changes in skin colour across the six articles revealed consistent trends while also highlighting variations in the descriptions of these methods.

The choice of measuring tools varied among the studies, with some utilising chromameters (colorimeters), spectrophotometers, and one using spatial frequency domain imaging. Studies using colorimeters justified their choice based on cost-effectiveness and satisfactory accuracy for their specific research questions (17,24,26), while those opting for spectrophotometers emphasised their slightly higher accuracy and the ability to measure colour across small wavelength intervals, facilitating a broader investigation and analysis (21,22,25). Notably, article 4 compared the use of spatial frequency domain imaging with a colorimeter, employing the latter as a control (24).

The level of detail in describing the measurement methods varied among the articles. One article provided a comprehensive account, detailing standardised methods such as low-pressure masks, standardised lighting, CIE 2-degree standard observer, and the spectral range for measurements (21). However, other articles did not provide such detailed descriptions, lacking information on specific lighting and standard observer settings. While some mentioned minimising pressure on

the skin and calibrating devices between measurements (17,25), several articles omitted details on standardisation procedures (22,24,26). This divergence may stem from differing priorities in the methodologies, as some articles may have emphasised other aspects more relevant to their research questions.

Many articles focused on anatomical areas with minimal sun exposure to measure constitutive pigmentation, enabling comparisons before and after exposure to external factors (17,21,24–26). Universally, the non-sun-exposed areas were either the inner forearm or the buttocks. One article also measured a frequently sun-exposed area using the outer forearm (17). With the exception of one study (24), all conducted three measurements per site, utilising the average for analysis.

All articles conducted measurements using the CIELAB colour space, with one article incorporating measurements in the RBG colour model as an additional colour space (25).

The Purpose of Colour Measurements in each Original Article

The objective behind conducting colour measurements varied across the studies.

In Article 1, the aim was to compare the baseline colour composition with changes induced by the application of DHA tanning gel, evaluating colour alterations at 4 hours (4h) and 24 hours (24h) post-application. The study sought to understand how the colour transformation with the tanning gel differed from a natural tan (21).

Article 2 focused on assessing colour changes resulting from the application of thermal cream and a skin-blanching cream in both Caucasian and African groups. This allowed for a comparative analysis. Additionally it considered clinical presentations of irritation through symptoms and visual signs between the two groups (17).

Article 3 utilised measurements to calculate the Individual Typology Angle (ITA) for each Fitzpatrick skin phototype assigned to participants subjectively. The study also evaluated the tanning differences among various Fitzpatrick skin phototypes. Notably, the instrument was not

employed to assess colour changes after the introduction of an external factor; instead, other non-spectrophotometer-related changes were the target of interest in this study (22).

Article 4 used the colorimetric measurements to compare with measurements conducted by spatial frequency domain imaging (24).

Article 5 used measurements to calculate the ITA of participants objectively, aiding in the assignment of a Fitzpatrick skin phototype. However, the study did not involve a comparison of colour changes after introducing an external factor (25).

Article 6 used the measurements to assess the compositional colour changes before and after visual light irradiation, comparing it across a range of melanin pigmentation (26).

Summary of Method of Statistical Analysis of Original Articles

The choice of statistical analysis method varied depending on the research question addressed in each article. For studies assessing colour change, standard formulas for the CIELAB colour space were employed to calculate chroma, ΔE (colour variation), and ITA (17,21).

Chroma:

$$C^*_{ab} = \sqrt{a^{*2} + b^{*2}}$$

Variation of colour:

$$\Delta E = \sqrt{(\Delta a^{*2} + \Delta b^{*2} + \Delta L^{*2})}.$$

ITA:

$$ITA = \tan^{-1}\left(\frac{L^* - 50}{b^*}\right)\frac{180}{\pi}\,[\mathrm{deg}]$$

Two articles utilised ITA to objectively categorise participants in a manner comparable to Fitzpatrick skin phototypes. However, each article used slightly different criteria for their respective groups.

In Article 1 (21) skin colour is classified by ITA into categories such as “Very Light Skin” (VLS), “Light” (LS), “Intermediate” (IS), “Tan” (TS), and “Brown” (BS), with the following criteria:

- VLS: ITA > 55°
- LS: 55° > ITA > 41°
- IS: 41° > ITA > 28°
- TS: 28° > ITA > 10°
- BS: ITA < 10

In article 6 (26) skin colour is classified by ITA into the following categories:

- Light: ITA > 41
- Intermediate: 10 ≤ ITA ≤ 41
- Dark: ITA < 10

The other 3 articles used varied statistical programs, such as SPSS, to find linear correlations between their factors in question (22,24,26).

All the articles had defined their p-value for statistical significance to be $P < 0,05$.

Comparing Results

Although the outcomes vary among the articles, their exact results are not central to my research question. What holds significance is the reliability and accuracy of these results. The observed reliability contributes to the reinforcement of my hypothesis that colorimetry is a valuable method for clinical applications in dermatology.

Article 1: A colorimetric comparison of sunless with natural skin tan

Amano et al. (21) discovered a significant shift in colour after applying DHA tanning gel, which was analysed through graphs and confirmed with a one-way ANOVA and subsequent t-tests.

- “One-way ANOVA comparing 0h, 4h, 24h: $F(2, 297) = 505.4$, $p < 0.05$; t-tests: 0h vs. 4h: $t(198) = 10.9$, $p < 0.05$; 4h vs. 24h: $t(198) = 30.9$, $p < 0.05$” (p. 9).

These results, both the overall comparison (ANOVA) and the specific pairwise comparisons (t-tests) confirm that there are statistically significant differences in DHA-induced shifts between the different time points (0h, 4h, 24h) (21). The statistical significant difference strengthens my hypothesis that spectrophotometers are capable of assessing if there is a significant colour change. However, one needs to be aware of the fact that this study underwent measurements on Caucasian skin (21).

Article 2: Chromometric assessment of drug skin tolerance: A comparative study between Africans and Caucasians skins

Sounouvou et al. (17) found results that are more relevant to my research question. They provide evidence of aspects to be aware of when measuring colour change in melanin-rich skin in comparison to Caucasian skin.

- “Skin brightness, constitutive L* values were lower ($P < .0001$) in Africans (40.82 ± 4.93) than in Caucasians (66.72 ± 1.44) with a 95 percent confidence interval (95% CI) of difference at -29.5 to -22.3” (p.332). This confirms the fact that African skin is perceived darker than caucasian skin.
- “No significant difference was found in b* values between both ethnic groups (16.15 ± 3.42 for Africans vs 15.29 ± 1.39 for Caucasians, $P = 0.5$)” (p. 332). Presenting the fact that there is no significant difference in the yellow tone between the two ethnicities.
- “Africans exhibited a higher (11.13 ± 0.96 vs 7.93 ± 1.14 for Caucasians; $P < .0001$) value of a* (95% CI of difference with Caucasians = +2.2 to + 4.2) compared to Caucasians” (p. 332). This is an important fact to consider as it provides evidence that Africans have redder skin than caucasians in their baseline.

These results show how data collected by a colorimeter, can break down the colour composition of the skin and analyse several aspects simultaneously, e.g. specifically looking at *a (erythema).

After the irritation test, one African participant showed no irritation symptoms, while others had moderate irritation. All the Caucasian participants experienced irritation. Fisher's exact test showed no significant difference in irritation proportions between Africans and Caucasians (P = 0.09) (17).

At the irritated sight for the African participants:

- "There was no significant difference observed for parameter L*" (p. 333).
- "Significant increase in parameter a* was observed" (p. 333).
- "Global skin colour variation (ΔE) was significantly more important at African irritated sites" (p. 333).
- "Δb* was significantly lower at irritated sites versus control ones" (p. 333).

At the irritated sight for caucasians:

- "Δa* and ΔE had higher values and L* decreased" (p. 333).
- "The b* parameters, unlike the observations made in Africans, slightly increased" (p. 333).

Though a significant difference was found with the participants with moderate to severe irritation, the African participants with slight irritation did not have a significant increase in *a. Providing evidence that colorimeter is less sensitive to detect slight changes in *a in highly pigmented skin. There were no Caucasian participants with slight irritation (17).

Article 3: Melanin has a Small Inhibitory Effect on Cutaneous Vitamin D Synthesis: A Comparison of Extreme Phenotypes

Young et al. (22) did not use the readings obtained from spectrophotometry to assess any colour change. Their study focused on if melanin concentration had an impact on vitamin D synthesis. They discovered a significant association between ITA and 25(OH)D3 response to SSR (solar simulated radiation) in habitually exposed and sun-protected skin sites.

- "Exposed skin: r = -0.886, P = 5.53 x 10^(-17)" (p. 1419).
- "Protected skin: r = -0.881, P = 1.44 x 10^(-16)" (p. 1419).

Despite the association with ITA, Fitzpatrick skin phototype (FST) had a stronger relationship with 25(OH)D3 response to SSR.

- “FST correlation: r^2 = 0.821, P = 0.001007” (p. 1419).

Results indicate that using Fitzpatrick Skin Type in evaluating the relationship with vitamin D has a stronger statistical association than using ITA (colorimetry). The findings suggest that when evaluating the relationship between skin characteristics and vitamin D synthesis, FST may be a more reliable parameter than ITA (22).

Article 4: Quantifying the confounding effect of pigmentation on measured skin tissue optical properties: a comparison of colorimetry with spatial frequency domain imaging

Phan et al. (24) compared the use of spatial frequency domain imaging (SFDI) with the use of a colorimeter. Though it tackles an instrument that is not central to my research question it uncovered some interesting results that are worth including.

The results in this study found that μs (scattering) and μa (absorption) were affected differently by the increased melanin in the darker skin group, at different wavelengths. The observed differences in scattering properties between darker and lighter skin suggest variations in tissue composition, with darker skin showing lower scattering values, especially at shorter wavelengths (24).

- “Differences in measured μs between the two *L groupings decreased with increasing wavelength, and at 851 nm there was only a 10% difference in measured μs between the two groups for both the ventral forearm and palm” (p. 5).
- “The ventral forearm, in subjects with dark skin, exhibit a strong negative correlation between measured μa and μs in the visible regiment (R = −0.93 at 471 nm; R = −0.88 at 659 nm). This correlation does not persist at 851 nm (R = −0.024)” (p. 5).

The difference between dark and light skin decreases with increasing wavelength, indicating that

longer wavelengths are less affected by skin pigmentation.

- “In the ventral forearm, there is a very strong positive correlation between *L and measured μs at 471 nm (R = 0.97) and 659 nm (R = 0.92)” (p. 6).
- “Lower *L values correspond to darker skin tone, so the positive correlation between *L and measured μs at visible wavelengths implies that tissue scattering values measured with SFDI are underestimated for patients with darker skin” (p. 6).

The findings highlight potential underestimation of tissue scattering in patients with darker skin, which is crucial for accurate optical property assessments.

Article 5: Risk of Migraine in Europeans with Low Melanin Levels —A Population Based Case-Control Study

Kobus et al. (25) assessed the correlation between skin tone and occurrence of migraines.

- “ANCOVA analysis revealed significant relationships between lower MI (melanin index) and the prevalence of migraine in both women and men ($p = 0.002$, $p = 0.032$, respectively)” (p. 4).
- “Women with MI < 28.56 had a 3.5-fold increased risk of migraine (OR 3.53, 95% CI 1.80–6.90, $p < 0.001$)” (p.4).
- “Men with MI < 27.68 had a 3.7-fold increased risk of migraine (OR 3.73, 95% CI 1.43–9.73, $p = 0.007$)” (p. 4).

The study suggests a significant association between lower melanin levels (fairer skin colour) and an increased risk of migraine in both women and men.

The study also underwent a comparison of spectrophotometric skin colour parameters in both study groups.

- “Erythema Index (EI): Women with migraine had a lower erythema index (EI) compared to controls ($p < 0.001$)” (p. 5).
- “L* Values: Women with migraine had higher L* values (lightness) compared to controls

(p = 0.002)" (p. 5).

- "a* Values: Women with migraine had lower a* values (green to red component) compared to controls (p = 0.001)" (p. 5).
- "R/G/B Values: Women with migraine had higher values of R (red), G (green), and B (blue) compared to controls (R: p = 0.002; G: p = 0.002; B: p = 0.004)" (p. 5).

Variations in erythema, lightness (L*), and colour components (a*, R/G/B) in women with migraine compared to controls indicate potential differences in skin physiology associated with migraine (25).

Though these results do not bring any evidence on assessing colour change, it does shed light on the use of spectrophotometer in research to produce significant and reliable results.

Article 6: Skin type specific photobiological response to visible light is mediated by constitutional melanin

Lim et al. (26) investigated the colour changes that occur after visible light radiation (400-700 nm wavelength), across a variety of skin tones.

<u>Pigmentation change in dark and intermediate skin type:</u>

- "Dark skin = 11% increase in pigmentation" (p. 334).
- "Intermediate skin = 8% increase in pigmentation" (p. 334).

<u>Erythemal response to visual light radiation:</u>

- "Light skin: increase in a* by 46%" (p. 334).
- "Intermediate skin: increase in a* by 26%" (p.334).
- "Dark skin: decrease in a* by 17%" (p. 334).
    - Note: This decrease might be influenced by increasing pigmentation (L*), impacting colorimetric readings rather than indicating a true reduction in erythema.

Tanning and skin type were moderately correlated:

- Fold change in L* and ITA: Correlation Coefficient (r) = 0.59, p = 0.02 (p. 334).

Erythema and skin type were strongly correlated:

- Fold change in a* and ITA: Correlation Coefficient r = 0.78, p = 0.006 (p. 334).

This study provides evidence that *L effects *a which is similar to article 2 (17) findings which indicated that the sensitivity of colorimetric measurement is reduced in darker skin.

Results from previous Meta-analysis

In this section, I will provide a summary of the two meta-analyses identified in my search. The emphasis will be on highlighting key points and presenting results relevant to my research question.

Meta-analysis 1: Photoprotection of the Skin from Visible Light–Induced Pigmentation: Current Testing Methods and Proposed Harmonisation

The purpose of the study was to compile evidence to propose a standardised method for assessing sunscreen protection against visual light (VL) radiation (23).

They compared in vitro, ex vivo and in vivo methods of assessing level of protection from visual light radiation. They had a total of 19 original articles that provided evidence for the three different methods (23).

Their findings were:

- “Cell-based in vitro studies are only suitable for screening compounds, and methods based on ROS should not be used to assess the protective effects against VL-induced hyperpigmentation” (p. 2573).
- “Ex vivo models can be useful to confirm preliminary results obtained in vitro, but they do not adequately assess persistent hyperpigmentation” (p. 2573).
- “In vivo models should be considered the gold standard. They provide the most accurate assessment of a sunscreen’s protection against VL in terms of persistent hyperpigmentation” (p. 2573).

Based on the evidence they uncovered, they presented a standardised protocol on how to test SPF-protection against VL across a range of skin-tones. In this protocol colorimetry assessment to determine ITA, was crucial to find the sunscreens protection factor against visual light radiation (23).

Meta-analysis 2: Research Techniques Made Simple: Cutaneous Colorimetry: A Reliable Technique for Objective Skin Colour Measurement

The purpose of this meta-analysis was educational. Outlining the general principles of colorimetry, usage and recommended protocol, and its application in research as well as clinically (9).

The article emphasises the importance of standardisation of measuring environment, and settings, as these devices are sensitive to environmental changes. It presents a protocol for the use of colorimeters to ensure reproducible results and reduce interfering factors. With regards to spectrophotometric instruments the article states that they have a high degree of accuracy and can measure absolute colour. However, it is equally as important to follow a standardised protocol to produce reliable results (9).

Based on this studies analysis of 38 articles they have concluded that:

- "Colorimetric devices are more reliable than subjective visual grading in assessment of cutaneous colour changes" (p. 9).
- "They enable greater accuracy in the determination of the minimal erythema dose" (p. 9).
- "They can detect erythematous and tanning responses of the skin that are below visual threshold and even in the presence of heavy pigmentation" (p. 9).

The limitations of colorimetric devices found through their analysis was:

- "Tristimulus colorimetric devices are limited in their ability to differentiate colours with identical perceived appearance, but different spectral features" (p. 10).
- "Standard protocol needs to be used to produce reliable, comparable results. Specifications for each of these settings need to be stated:

- Illuminant
- Standard observer
- Measurement system
- Specular component
- Measuring geometry" (p. 10)

Summary of all the Results

In summary, the articles in the study employed colorimeters or spectrophotometers across various skin tones, yielding statistically significant results. These instruments demonstrated effectiveness in capturing detailed colour compositions of the skin irrespective of pigmentation levels. However, certain limitations were identified, such as challenges in detecting subtle changes in *a (erythema) for darker skin tones (17). Additionally, questions arose regarding the potential influence of *L (lightness) on *a, introducing a consideration for potential errors in interpreting *a (erythema) (26). The meta-analysis further supported the value of colorimetry, but emphasised the importance of conducting measurements under standardised conditions.

DISCUSSION

Strengths and Limitations of the Methodology

Though the methodology chosen to find relevant articles was thorough and detailed it resulted in a narrow search. The search words chosen were perhaps too specific to include articles that could have been relevant. The strategy could have been improved, to include additional terms related to skin conditions or reduce the number of search words which could have resulted in a wider search that encompassed more relevant articles. Having a wider search originally then narrowing it down with relevant abstract could have allowed for a better selection of articles.

Restricting the search to English articles might introduce language bias. Considering the international nature of dermatological research, relevant non-English studies could be excluded. Additionally, limiting the search to the last 3 years may result in missing relevant older studies, especially if there is limited recent research on the topic. My decision to only include the last 3

years was based on the fact that medical technology has a short halflife and technological advances are made at a rapid pace.

The original articles found in my search were randomised control trials and a case-control study. These are methods that are reliable and produce results that minimise bias and interfering factors. The results of such studies are deemed strong and of great value within the research community. However, aspects such as sample size and control of the environment should be considered when interpreting the results. Many of the articles I included had a relatively small sample size, (17,24,26) making causation conclusions less reliable. There were also some articles that lacked detail in their methodology and control of the environment, which could introduce confounding variables, making their results less credible (22,24,26).

The articles that were included in the study were not all of great relevance or value to the original research question. Many of the original articles studied topics that ventured beyond what was deemed relevant to the question at hand. This made comparison of methodology and results challenging. The articles that provided valuable results to strengthen my hypothesis were articles 2, 4 and 6 (17,24,26).

Comparison with Existing Data

Article 2, 4 and 6 (17,24,26) provided evidence that answered aspects of my research question. Article 2 (17) sheds light on the fact that a colorimeter is not sensitive enough to detect slight irritation, which leads to slight increase in *a (erythema) in highly pigmented skin. It does provide evidence that a colorimeter is able to detect a significant difference in *a at a moderate to severe irritation in highly pigmented skin. In clinical practice a colorimeter could be used in scoring PASI to avoid subjectivity and observer and recall bias. The PASI score is the foundation on which the clinician bases the decision of the treatment level the patient should receive. The patients that are in need of biological treatment and light therapy are the ones with moderate to severe disease. Therefore, the lack of sensitivity the colorimeter has on slight irritation will most likely not have a significant impact on the clinical outcomes.

Article 2 (17) shows that African skin has a constitutional increased *a value. This is a factor to consider if implementing colorimetry in a clinical setting, as different sets of reference values based on different ethnicities might be necessary. This is an aspect that should be considered in further research.

Article 6 (26) included findings that in dark skin *a might be influenced by increasing pigmentation (*L - lightness). Contrary to what was expected, *a decreased when exposed to radiation (visible light in the wavelength range 400-700 nm) in dark skin. At the same time *L decreased due to the radiation. This suggests that low level of *L (darker skin) interferes with the measurement of *a in darker skin tones. These results strengthen what has been observed in article 2 (17) which had findings that indicated the sensitivity of colorimetric measurement is reduced in darker skin.

Though article 4 (24) uses spatial frequency domain imaging (SFDI) it highlights that measuring tools can cause systematic error if not all aspects of the difference in the skin is considered. The results the article presents shows that the composition of the skin varies with difference in melanin content. This is contrary to previous models on reflectability where the skin is considered a homogeneous mass. This model can work in Caucasian skin, but is not transferable to melanin-rich skin. This systematic error occurs mostly at shorter wavelengths and gets cancelled out at longer wavelengths. This highlights the importance of a standardised light source when conducting measurements. And sheds light on the aspect that methods used in Caucasian skin cannot automatically be transferred over to melanin-rich skin.

Article 1, 3 and 5 (21,22,25) do not directly answer my research question in any way. They do show that there are many aspects where colorimetry and spectrophotometry can be used, but venture outside the scope of this study. They have, however produced statistically significant results that strengthen the fact that colorimeters and spectrophotometers are reliable methods of investigation. However, they did not provide enough evidence to conclude that colorimeters are a better tool to assess erythema than visual grading to avoid skin pigmentation bias.

Implications and Significance

An aspect that was evident in many of the articles, especially article 1 and 2 (17,21) and meta-analysis 1 and 2 (9,23) was the need for standardisation of the methodology. A potential limitation in using colorimeters is not using a standard protocol to undergo measurements. This leads to the results not being comparable, and in research does not allow for reproducible results. Therefore, it is important to be in the same environment, using a standard illuminant, standard observer, calibrated colorimeter and ensure the patient has not undergone any rigorous strain within 30 minutes prior to the measurements. This is something that needs to be considered in further research on this topic.

Diving into the technology of colour measuring instruments, I have uncovered many tools that could be used to score erythema in an objective way. As of today a colorimeter is a good choice for clinical use. However, as the technology develops other tools such as spectrophotometers might be more suitable.

Some aspects such as methods to reduce variables when conducting measurements using colorimeters, have been addressed. Many of the articles and meta-analyses provide evidence on aspects that are important to keep in mind when designing a standardised methodology. The question of the accuracy of using colorimeters compared to the clinical method used today has not been answered in a complete manner. This leaves room for a focused investigation to answer this question fully.

Through the heterogeneous nature of the articles I have investigated, all show that colorimeters and spectrophotometers can be used in a large range of clinical situations. There is a huge potential to improve our clinical methods and remove as much human error and bias as possible, if we are open minded to use technology to our advantage.

CONCLUSION

Through the articles I have read and the evidence I have found, I can conclude that none of the articles explicitly provides adequate evidence to answer this question: How accurate is the use of

a colorimeter to grade erythema on melanin-rich skin compared to the subjective clinical method used today? A few of the articles present evidence that colorimetry is a more reliable method than assessing visually, however the degree of accuracy cannot be determined based on their results. Further research is needed to answer this question. Therefore, I present a protocol for further investigation into this topic. Hopefully this will provide evidence that can catalyse a change in the clinical practice at the Dermatological Department of Rikshospitalet, and bridge the gap between ethnicities and skin colour that is present today.

PROTOCOL

My original motivation when I started this thesis was to undergo a pilot study. The study would try to answer the question of the efficacy of colorimetry compared to the clinical method used at Rikshospitalet, in patients with melanin-rich skin. To uncover if there is a gap in the treatment being offered to patients due to their skin pigmentation. I was unable to conduct such a study in the time frame given. However, I would like to suggest this protocol on the basis of what I have learned, in the hope that I will be able to see this study through some time in the future.

Participants

A total of 24 participants with no underlying skin conditions or chronic illness are recruited for the study. 4 participants, 2 of each gender, from each Fitzpatrick skin phototype, are categorised with a self-assessment questionnaire. The age range of participants is between 18-50 years old. Each participant acts as their own control.

Materials

The colorimeter used for the measurements is the Delfin SkinColorCatch. Images of the test area are taken by the DermLite DL5 with the MCC smartphone adapter, connected to a smartphone. A 2.0% Sodium Lauryl Sulphate (SLS) in an aqueous solution is used to provoke irritation of the skin.

Test Protocol

Before the test is conducted, it is ensured that none of the test participants have undergone any rigorous activity within the last 30 minutes. The test is conducted on the inner forearm of each participant. A square grid is used to identify the test and control area, which is at least 4 cm apart. Hair, naevi, scars, and visible blood vessels are avoided. The test and control area are 1x1cm squares.

All colorimetric measurements are conducted in a windowless room with the temperature being between 19-25 degrees Celsius. The Delfin SkinColorCatch is calibrated with a white standard before each measurement. The standard illuminant, illuminant D65, is used, as well as CIE 2. Degree standard observer. The readings are conducted while holding the colorimeter perpendicular to the test site, avoiding any additional pressure on the skin. Three measurements are taken at each site, and the average of these is used in the calculations. All measurements are presented in the CIELAB colour space.

The measurements of the control area are conducted first. At the test area, 2 drops of SLS solution are added to the surface of the skin. The solution is left on the site for 30 minutes before removing, avoiding any scrubbing of the skin. Colorimetric measurements are conducted as described.

The DermLite DL5 with the MCC smartphone adapter, connected to a smartphone is used to take dermatoscopic pictures of the test site that are assessed by an independent dermatologist to provide a score of erythema.

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