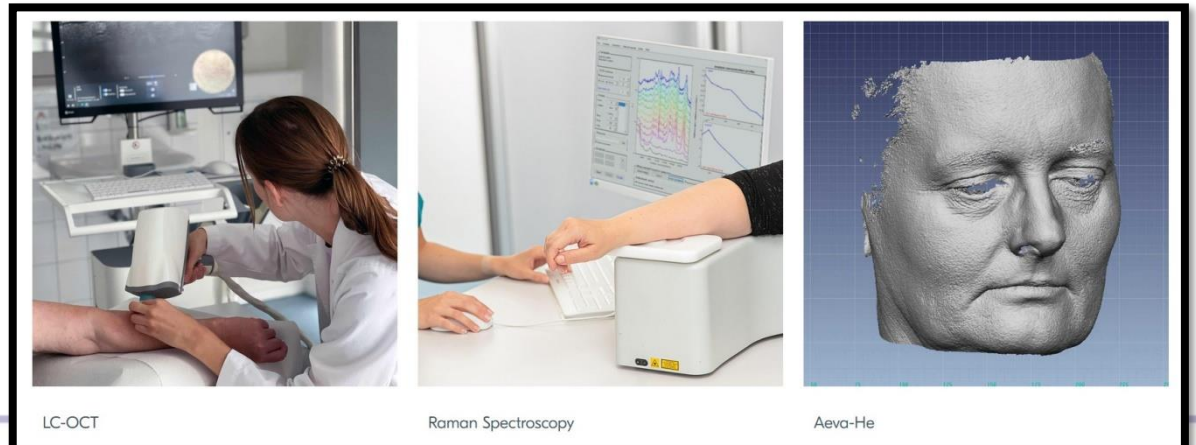
Kliničko testiranje kozmetičkih proizvoda: potvrda reklamnih tvrdnji kroz procenu efikasnosti i bezbednosti

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Review Article Open Access

Guidelines on Cosmetic Efficacy Testing on Humans. Ethical, Technical, and Regulatory Requirements in the Main Cosmetics Markets

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Abstract

The main regulatory frameworks governing the cosmetic industry dates back to 1938 in the United States (US) and 40 years later in Europe (EU). Since then, both the US and EU cosmetic legislations have inspired the regulatory framework of a number of countries working toward harmonisation of cosmetics legislation. During the years the requirements for the efficacy of cosmetic products have been implemented to adapt them to the state of the art; however no clear guidelines for efficacy testing on cosmetic products exist. The lack of guidelines and/or shared position on cosmetic testing represents the missing link between the regulatory requirements and the consumer protection from misleading claims in the real life. On the other side a regulatory claimed prerequisite is ineffective if clear and specific testing methodologies are not available to the cosmetic industry. This introduce a discretionary element decreasing the strength of the original regulatory requirement, having an impact on consumer protection from misleading claims, and sometimes decreasing the credibility of the cosmetic product in the marketplace. Initiatives aimed at developing clear, specific for cosmetic products, and effective guidelines should arrive from the academy, industry, and professional associations. This manuscript is aimed to give an overview of the main ethical, technical and regulatory concerns affecting the design of an efficacy study carried out on humans.

Keywords: Cosmetics; Efficacy testing; Regulatory framework; **Ethical requirements**

Zakonski okvir u EU i RS?

- Kozmetička Uredba EC 1223/2009

Article 20

Product claims

1. In the labelling, making available on the market and advertising of cosmetic products, text, names, trade marks, pictures and figurative or other signs shall not be used to imply that these products have characteristics or functions which they do not have.

2. The Commission shall, in cooperation with Member States, establish an action plan regarding claims used and fix priorities for determining common criteria justifying the use of a claim.

After consulting the SCCS or other relevant authorities, the Commission shall adopt a list of common criteria for claims which may be used in respect of cosmetic products, in accordance with the regulatory procedure with scrutiny referred to in Article 32(3) of this Regulation, taking into account the provisions of Directive 2005/29/EC.

By 11 July 2016, the Commission shall submit to the European Parliament and the Council a report regarding the use of claims on the basis of the common criteria adopted under the second subparagraph. If the report concludes that claims used in respect of cosmetic products are not in conformity with the common criteria, the Commission shall take appropriate measures to ensure compliance in cooperation with the Member States.

3. The responsible person may refer, on the product packaging or in any document, notice, label, ring or collar accompanying or referring to the cosmetic product, to the fact that no animal tests have been carried out only if the manufacturer and his suppliers have not carried out or commissioned any animal tests on the finished cosmetic product, or its prototype, or any of the ingredients contained in it, or used any ingredients that have been tested on animals by others for the purpose of developing new cosmetic products.

- Uredba EC o tvrdnjama/zajednički kriterijumi za opravdavanje tvrdnji u vezi sa kozmetičkim proizvodom (KP) 655/2013

COMMISSION REGULATION (EU) No 655/2013
of 10 July 2013
laying down common criteria for the justification of claims used in relation to cosmetic products
(Text with EEA relevance)

1. Usklađenost sa zakonom
2. Istinitost
3. Dokazni materijal
4. Poštenje
5. Pravednost
6. Odlučivanje na osnovu informacija

- Okvir formiranja tvrdnji za kozmetičke proizvode
- Nisu usmereni ka preciznom definisanju i određivanju načina izražavanja tvrdnji

Hronologija i hijerarhija

Centar za kozmetologiju i dermofarmaciju

1.

COMMISSION REGULATION (EU) No 655/2013

of 10 July 2013

laying down common criteria for the justification of claims used in relation to cosmetic products

(Text with EEA relevance)

2.

Brussels, 19.9.2016
COM(2016) 580 final

REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on product claims made based on common criteria in the field of cosmetics

3.

Technical document on cosmetic claims

Agreed by the Sub-Working Group on Claims

(version of 3 July 2017)

Stupio na snagu 1. jula 2019.

4.

GUIDELINES FOR COSMETIC PRODUCT CLAIM SUBSTANTIATION

Revising and expanding the Colipa Guidelines on Efficacy (2001/rev. 2008)

22 May 2019

[1] The Working Group is chaired by the European Commission and is composed of representatives of all Member States of EU and EFTA, the European Consumer Organisation (BEUC), The Personal Care Association (Cosmetics Europe), the European Federation for Cosmetic Ingredients (EFfCI), the International Fragrance Association (IFRA), the European Organisation of Cosmetic Ingredients Industries and Services (Unitis), the European Association of Craft, Small and Medium-sized Enterprises (UEAPME), the International Natural and Organics Cosmetics Association (Natrue), and the European Cosmetics Responsible Person Association (ERPA).

Nacionalni propisi – zahtevi / Pravilnik o KP

- 2. ДОКУМЕНТАЦИЈА ОД ЗНАЧАЈА ЗА ДОКАЗИВАЊЕ БЕЗБЕДНОСТИ КОЗМЕТИЧКОГ ПРОИЗВОДА
- **Досије са информацијама о производу**
- Члан 4.
- Досије са информацијама о производу (у даљем тексту: Досије) садржи редовно ажуриране информације и податке и то:
- 1) опис козметичког производа који омогућава недвосмислено и јасно повезивање Досијеа са одговарајућим козметичким производом;
- 2) извештај о безбедности козметичког производа у складу са Прилогом 1.;
- 3) опис методе производње и изјаву о усклађености са добром произвођачком праксом, у складу са законом који уређује област предмета опште употребе;
- **4) доказ тврдње о постојању ефекта који има козметички производ, уколико је то оправдано према природи ефекта козметичког производа;**
- 5) податке о свим тестирањима на животињама извршеним од стране произвођача, његових заступника или добављача, у сврху процене безбедности козметичког производа или његових састојака, укључујући било која тестирања на животињама извршена како би се испунили регулаторни захтеви других земаља.
- Прилог 1. из става 1. тачка 2) овог члана одштампан је уз овај правилник и чини његов саставни део.

Nacionalni propisi – zahtevi / Pravilnik o KP

5. ТВРДЊЕ КОЈЕ СЕ КОРИСТЕ У ВЕЗИ СА КОЗМЕТИЧКИМ ПРОИЗВОДИМА

Члан 16.

Тврдње (у облику текста, имена, жигова, слика и симболичних или других ознака) којима се експлицитно или имплицитно наводе обележја или функције козметичког производа, морају бити у складу са одредбама овог правилника и могу се употребљавати приликом означавања, стављања у промет и рекламирања козметичког производа, независно од медија или врсте употребљеног маркетиншког алата, назначених функција производа и циљне групе.

Члан 17.

Одговорно лице, у складу са одредбама Закона које се односе на одговорно лице за козметички производ, обезбеђује да је текст тврдње у вези са козметичким производом усклађен са заједничким критеријумима за тврдње наведеним у Прилогу 10. који је одштампан уз овај правилник и чини његов саставни део.

Одговорно лице обезбеђује да је текст тврдње у вези са козметичким производом усклађен и са документацијом која доказује тврдњу о постојању ефекта који има козметички производ, а која је саставни део Досијеа са информацијама о производу из члана 4. овог правилника, односно Документације са информацијама о производу из члана 5. овог правилника.

ПРИЛОГ 10. – ЗАЈЕДНИЧКИ КРИТЕРИЈУМИ ЗА ТВРДЊЕ НА КОЗМЕТИЧКИМ ПРОИЗВОДИМА

Efekti kozmetičkih proizvoda: = ili ≠ efikasnost?

Primena kozmetičkih proizvoda na koži/adneksima kože može proizvesti različite (pozitivne) efekte:

- Poboljšanje vlažnosti – stepena hidratisanosti SC-a/kose
- Poboljšanje barijerne funkcije kože
- Glatkiji mikroreljef kože/glatkiju teksturu vlasi
- Revitalizovanje mehaničkih svojstava kože
- Smanjenje ljuspanja kože
- Uticaj na sadržaj lipida na površini kože/kose
- Korekcija pH kože
- Promena boje kože
- Smanjenje stepena iritacije kože…

Šta može da se tvrdi kod KP?









Tvrdnje: definicija i tipovi – Vodič Cosmetics Europe – na bazi svih relevantnih EU propisa

- **Tvrdnje o KP** – generalno lako dostupni podaci - primarno u marketinške svrhe – o sadržaju, tipu KP, efektima, svojstvima ili efikasnosti KP.
- Sastoje se od teksta, naziva, trgovačkih oznaka, slika, simbola, ili drugih znakova, koji se mogu naći na pakovanju KP, u okviru deklaracije, umetnutog materijala, ili pri oglašavanju (npr. na mestu prodaje, u medijima…)

Različiti tipovi tvrdnji i kombinacije:

1) Tvrdnje performansi (tvrdnje vezane za efikasnost proizvoda, npr. vlažeći efekat, redukcija bora, zaštita od sunca…)

- Priroda testa (**objektivna** studija efikasnosti, percepcija korisnika (testovi za korisnike KP), in vitro/ex vivo testovi…
- Relevantnost testa treba da se objasni u postupku potkrepljenja tvrdnje
- Rezultati se obrađuju/validiraju statistički uzimajući u obzir uzorak ispitanika

Tvrdnje: definicija i tipovi

2) Tvrdnje bazirane na prisustvu sastojka (tj. vezane za sadržaj, svojstva, mehanizam delovanja, patentnu zaštitu…)

- Ne može svojstvo kozmetičkog sastojka direktno implicirati svojstvo/efekte/efikasnost KP: potrebni adekvatni i verifikovani dokazi, npr. demonstriranje prisustva sastojka u efektivnoj koncentraciji
- Sva svojstva koja se ističu kroz tvrdnje treba da su podržana **tehničkim obrazloženjem koje može da uključi studije ili generalno prihvaćene podatke**; **relevantnost ovih podataka za finalni proizvod mora da bude opravdana (npr. koncentracijom, sistemom za isporuku, tipom formulacije**…)
- **Tvrdnja o odsustvu sastojka treba da se demonstrira adekvatnim i verifikovanim dokazom; može da bude dokumentovana informacija, nije neophodan analitički dokaz**

Tvrdnje: definicija i tipovi

3) Senzorne tvrdnje: procena relativnog nivoa senzornog atributa (npr. lepljivost, masnoća, proizvod se lako upija) od strane obučenog eksperta – na relevantnoj skali, bez prosuđivanja o privlačnosti atributa

4) Tvrdnje vezane za percepciju korisnika: procena preko upitnika na ciljanom uzorku populacije korisnika o ličnom utisku/doživljaju koji se može vezati za atribute performansi ili senzorne atribute KP

5) Tvrdnje poređenja: poređenje sličnih proizvoda – poštovanje fer principa!
- Poređenje pre/nakon primene KP: vizuelno predstavljanje bi trebalo da bude proporcionalno i da koherentno reflektuje performanse proizvoda i da bude reprezentativno za testirani uzorak; poređenje u odnosu na konkretan KP sa navedenim serijskim brojem.

Tvrdnje: definicija i tipovi

6) Tvrdnje vezane za životnu sredinu: podležu zahtevima iz člana 20 EC Kozmetičke Uredbe 1223/2009

7) Tvrdnje vezane za životni stil, lične vrednosti & benefite (KP za posebne grupe korisnika – vegani, halal sertifikat, prirodna i organska kozmetika). Na njih se takođe odnosi 6 zajedničkih kriterijuma, potreba da korisnik na osnovu njih donese informisanu odluku/izbor; ne bi trebalo da ukaže na bilo koji benefit za korisnika, sem onog koji je zasnovan na činjenicama (npr. ne treba tvrditi da je proizvod bezbednji jer sadrži prirodne sastojke).

- Potrebno je sprovesti **odgovarajuće sertifikacije.**

8) Tvrdnje sa primenom hiperbole/namernog preuveličavanja:

Tvrdnje jasnog preuveličavanja/naduvavanja, koje ne traže potkrepljenje i jasne su prosečnom korisniku – dozvoljene su i ne zahteva se neke posebna vrsta dokaza.

Tvrdnje: nivo dokaza/dokaz za potkrepljivanje

Tvrdnje treba da su podržane pouzdanim, relevantnim i robustnim dokazom. Ovaj dokaz može da bude baziran na generalno prepoznatim podacima, internim ili eksternim eksperimentalnim studijama (instrumentalne/biohemijske metode, procena od strane ispitivača, senzorne procene, *in vitro* i *ex vivo* studije) i procene od strane korisnika.

Odluka o vrsti metodologije koja će se sprovesti za dokazivanje tvrdnje - na proizvođaču!

- **NE POSTOJI ZVANIČNA LISTA ODOBRENIH METODA - NE PRAVI SE RAZLIKA IZMEĐU SUBJEKTIVNIH, OBJEKTIVNIH, USTANOVLJENIH METODA ILI NOVIH POSTUPAKA OGLAŠAVANJA – SVE NA BAZI relevantnih, pouzdanih i reproduktivnih dokaza.**

- **TVRDNJA/NIVO TVRDNJE – USKLAĐEN SA NIVOOM DOKAZA!**

Tvrdnje: nivo dokaza/dokaz za potkrepljivanje

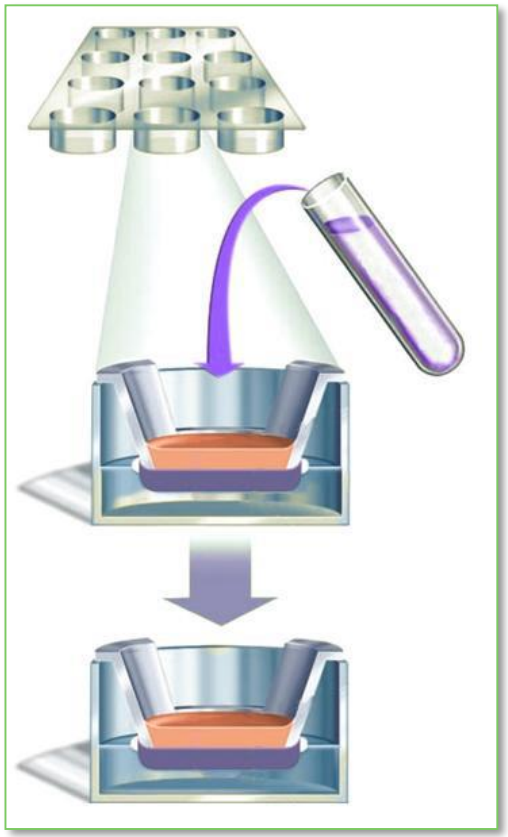
Od interesa za male proizvođače – GENERALNO PRIHVAĆENI PODACI (GPP)!?

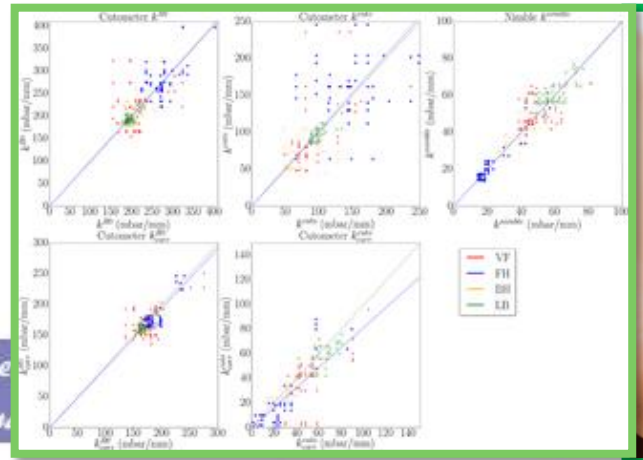
- Generisanje novih podataka da se podrži tvrdnja nije uvek neophodno, ukoliko su na **raspolaganju** **generalno prihvaćeni podaci (GPP)**
- Relevantnost ovih podataka za proizvod i tvrdnju mora se pokazati/opravdati, ukoliko se ovi podaci koriste kao dokazni materijal!
- **GPP – često nisu dovoljni , izuzev u slučaju najjednostavnijih tvrdnji, ali mogu biti deo dokaza u kombinaciji sa manjim obimom kvantitativnih podataka, da bi se tvrdnja podržala adekvatno!**
- **TRI BITNA RAZMATRANJA DA SE OVAJ VID POTKREPLJENJA PRIHVATI:**

1) **IZVOR PODATAKA**
2) **RELEVANTNOST POTKREPLJENJA ZA DATI PROIZVOD/TVRDNJU**
3) **TAČNOST PODATAKA.**

Tehnički dokument o kozmetičkim tvrdnjama, ***Annex II***
Najbolja praksa za prikupljanje dokaza za potkrepljenje tvrdnje

- Različiti tipovi dokaza mogu da se koriste da potkrepe tvrdnje, uobičajeno:
- eksperimentalne studije (*in silico*, *in vitro, ex vivo, in vivo*) – ZLATNI STANDARD
- testovi percepcije/opažanja korisnika
- publikovane informacije
- kombinacija svih prethodnih mogućnosti.







Guidelines for the evaluation of the efficacy of cosmetic products (Cosmetics Europe, 2009)

1) ***In vivo*** **senzorni testovi na humanim dobrovoljcima** (vizuelna, taktilna i olfaktorna procena od strane potrošača ili eksperata)

2) **Instrumentalni pristup baziran na *in vivo, ex vivo* ili *in vitro* testovima**

- ***In vivo instrumentalni testovi*** - na humanim dobrovoljcima (npr. klinička procena, merenja relevantnih biofizičkih parametara kože i retko, invazivne metode, kao što je biopsija kože)
- ***Ex vivo testovi ("off the living")*** - na biološkim supstratima koji su preuzeti iz živog organizma, bez modifikacije intrinzičkih svojstava (npr. izolovana vlas kose, izolovana humana koža, mikroflora kože, ili adhezivne trake koje su uklonjene sa površine kože
- ***In vitro testovi ("in glass")*** - sprovode se u laboratoriji, u veštačkim uslovima (npr. test tube, ćelijske kulture) - **uglavnom se koriste kao skrining instrumenti tokom razvoja proizvoda, ili za demonstriranje mehanizma delovanja kozmetičkih sastojaka**

Vodiči brojni…

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The science of Hair Care, Second edition, Edited by Claude Bouillon, John Wilkinson, Talor & Francis, 2005

Commission Recommendation of 22 September 2006 on the efficacy of sunscreen products and the claims made relating thereto (notified under document number C(2006) 4089) (2006/647/EC)

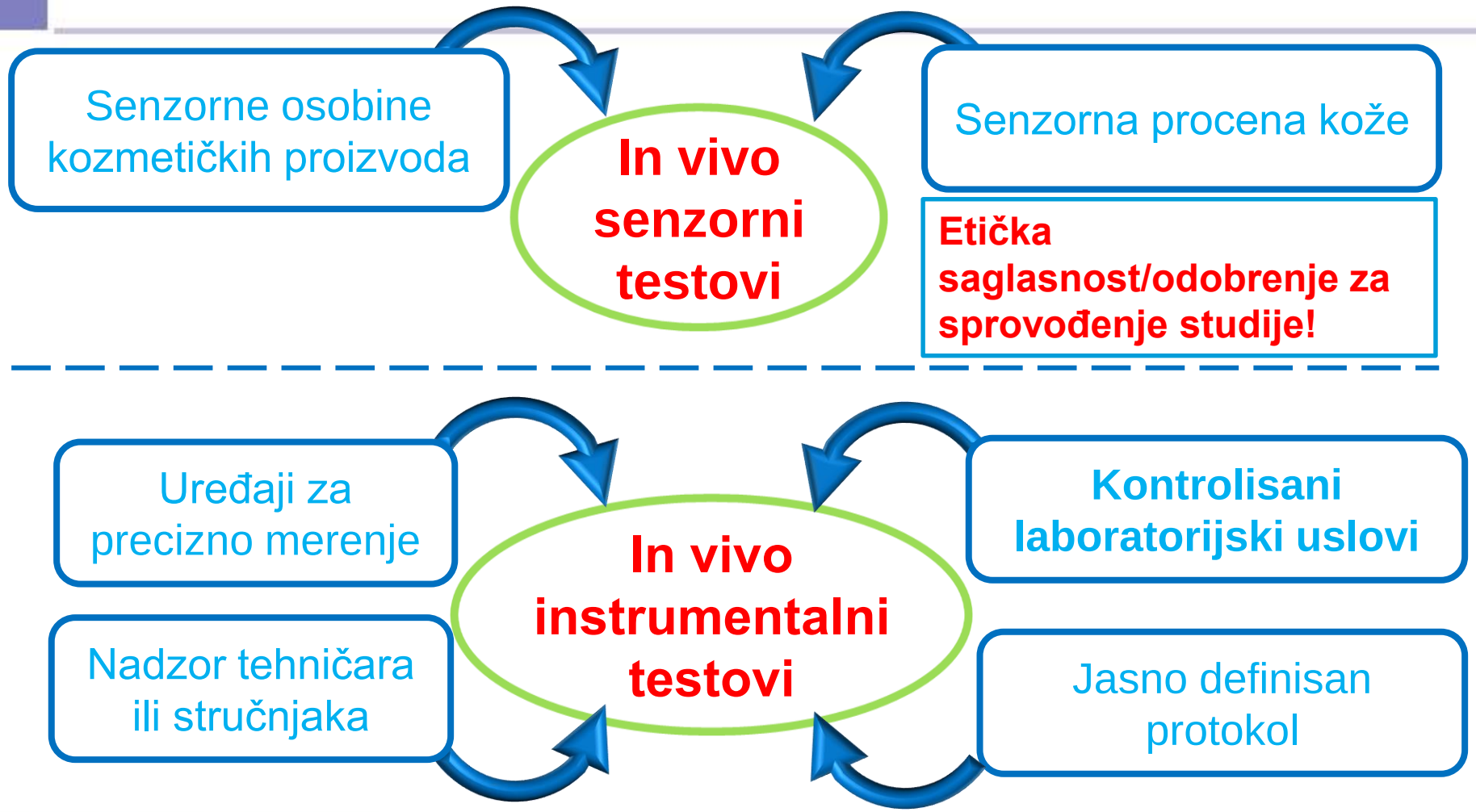
Ethnic Skin and Hair, Informa. Edited by Enzo Berardesca, Jean-Luc Leveque, Howard I. Maibach, 2007

Alternativni testovi za procenu efikasnosti – *in vitro*

Zahtevi:
Biološka relevantnost
Reproducibilnost
Visoka tačnost i preciznost
Pristupačnost
Jednostavnost



In vivo senzorni i *in vivo* instrumentalni testovi



Generalni zahtevi za optimalno sprovođenje svih in vivo tehnika za procenu parametara kože/biofizička merenja:

EEMCO (*European Group for Efficacy Measurements on Cosmetics and Other Topical Products*) - smernice

- sva ispitivanja treba izvoditi u laboratorijama sa konstantnom sobnom temperaturom (20-23°C) i relativnom vlagom od 40-60% (*air-conditioned*)
- ispitanici bi trebalo da se aklimatizuju na ove uslove u toku 30-tak min boravka u prostoriji gde se merenje obavlja
- psihološki i fiziološki uravnoteženi
- pogodno mesto za merenje je unutrašnja (volarna) strana podlaktice – nema malja
- poželjno je da osoba koja meri i procenjuje rezultate poseduje dosta iskustva
  (“*should be skilled in the art and possess a large amount of experience”*)

Najbolja praksa koja se primenjuje u eksperimentalnim studijama

- **Protokol studije mora biti validiran** da bi se obezbedilo da studija bude sprovedena i praćena na odgovarajući način, odnosno da se obezbedi kvalitetan nivo dokaza. Kakva god da je studija, **osoba koja je sprovodi** treba da:
- **-ima odgovarajuće kvalifikacije;**
- **-bude obučena i sa iskustvom u datoj oblasti istraživanja;**
- **-ima visoke etičke kvalitete/standarde i profesionalni integritet.**







Šta sve možemo instrumentalno da merimo od performansi kože? Mnogo toga, npr:

- Stepen hidratisanosti SC-a/vlažnost kože
- TEWL – kao meru barijerne funkcije kože
- pH kože
- Površinske lipide kože
- Melanin i eritem indekse – boju kože i stepen iritacije in vivo
- Biomehaničke, npr. viskoelastične karakteristike kože
- Mikroreljef i topografiju kože
- Čvrstinu kože
- Frikcija/trenje na koži
- Penetraciju/permeaciju kozmetički aktivne supstance ***in vivo*** (Raman spektroskopija)
- SPF i UVAPF – *in vivo/in vitro…*

TABLE 1 Description of the parameters analysed

Device	Parameters	Description	Units
Myoton Pro muscle probe Myoton AS, Tallinn, Estonia)	Biomechanical and viscoelastic properties	Axial elasticity (recovery rate after deformation) [17–20]	N/m
Myoton Pro Skin Probe Myoton AS, Tallinn, Estonia)	Biomechanical and viscoelastic properties	Tangential elasticity (recovery rate after deformation)[25–26]	N/m
Corneometer CM825 Corneometer MPA9, Courage & Khazaka, Germany	Capacitance	Hydration level of the SC of the epidermis [14–16]	AU
The Mexameter Courage & Khazaka, Germany	By reflectance	A receiver measures the reflection from the skin. As the quantity of emitted light is defined, the quantity of light absorbed by the skin can be calculated[16].	AU
TEWL, MPA9, Courage & Khazaka, Germany	TEWL	Evaporation rate from the skin [21–23]	g m−2 h−1

Abbreviations: AU, arbitrary units; TEWL, trans-epidermal water loss.

International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: Part 2. transepidermal water loss and skin hydration

TABLE 1. Commercially available TEWL measurement instruments in alphabetical order

Instrument	Measurement principle	Manufacturer
Aquaflux	Condenser type closed-chamber	Biox Systems Ltd, London, United Kingdom
AS-CT1	Unventilated closed-chamber type	Asahi Biomed Company Ltd, Yokohama, Japan
DermaLab	Open-chamber type	Cortex Technology, Hadsund, Denmark
Evaporimeter EP1 and EP2	Open-chamber type	ServoMed, Stockholm, Sweden
H4300*	Unventilated closed-chamber type	Nikkiso-YSI, Tokyo, Japan
Tewameter TM210 and TM300	Open-chamber type	Courage & Khazaka, Cologne, Germany
VapoMeter SWL3	Unventilated closed-chamber type	Delfin Technologies, Kuopio, Finland

*No longer manufactured (31).

TABLE 2. Commercially available skin hydration measurement instruments in alphabetical order

Instrument	Measurement principle	Manufacturer
ASA-M2	Conductance	Asahi Biomed Company Ltd, Yokohama, Japan
Corneometer CM820 and 825	Capacitance	Courage & Khazaka, Cologne, Germany
Dermalab Moisture Unit	Impedance	Cortex Technology, Hadsund, Denmark
MoistureMeter SC	Capacitance	Delfin Technologies, Kuopio, Finland
Nova Dermal Phase Meter DPM 9003	Impedance	Nova Technology Corporation, Portsmouth, NH, USA
Skicon 200 and 200 EX	Conductance	ISBS Co Ltd, Hamamatsu, Japan

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TABLE 3. Influence of endogenous-, exogenous- and environmental- and measurement-related factors on the measurement of TEWL and skin hydration

	TEWL		Skin hydration	
	Influence	References	Influence	References
Endogenous factors				
Age	Yes	(11, 39–41)	Yes	(11, 34, 41)
	No	(36–38)		
Gender	No	(11, 36, 42–45)	No	(11, 34, 44)
Ethnicity	Yes	(7, 46–48)	Yes	(49–51)
	Controversial	(11)	Controversial	(11, 16, 52)
	No	(43, 49, 50, 53, 54)		
Anatomical position	Yes	(7, 11, 38, 40, 48, 55–60)	Yes	(11, 28, 34, 41, 60, 61)
Skin temperature	Yes	(7, 9, 11)	Yes	(11)
Sweating	Yes	(9, 11, 62)	Yes	(11, 63)
Circadian rhythm	Yes	(11, 64–66)	Yes	(66)
			Controversial	(11)
	No	(58)	No	(64)
Skin health	Yes	(3, 59, 67–69)	Yes	(3)
Exogenous factors				
Skin washing and wet work	Yes	(70, 71)	Yes	(14, 71)
Solvents/Surfactants	Yes	(49, 50, 58, 72, 73)	Yes	(14)
Occlusion	Yes	(37, 57, 74, 75)	Yes	(1, 14)
			Controversial	(76)
Skin damage	Yes	(77, 78)	Yes	(74)
Caffeine (topical application)	Yes	(79)		
Smoking	Yes	(24, 80)	Yes	(81)
Environmental and measurement factors				
Air convection/movement	Yes	(9, 11)	Yes	(11)
Ambient temperature	Yes	(9, 11)	Yes	(11)
Relative humidity	Yes	(9, 11)	Yes	(11, 34, 61, 63)
Direct light	Yes	(9, 11)		
Season	Yes	(9, 11, 61, 82, 83)	Yes	(61, 84)
			Controversial	(11)

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1 Endogenous factors

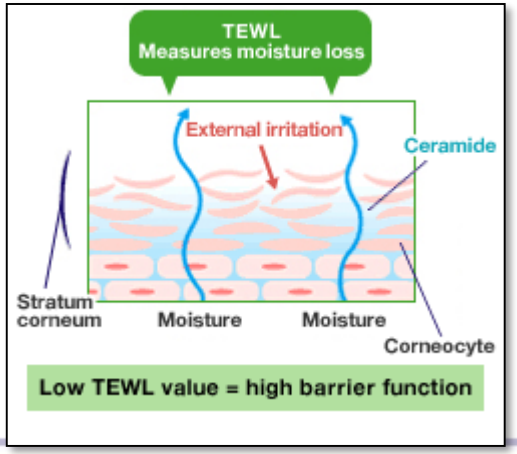
a The anatomical position(s) and exact site(s) of TEWL and/or skin hydration and a rationale for the choice of site(s).
b Skin health at time of measurements. For measurements on hands and wrists, health can be documented and assessed using, for example, a validated teledermatology toolkit for standardized hand photographs in non-clinical settings (98). Furthermore, the inclusion of a skin symptoms questionnaire for current symptoms might be advisable.
c Time of day when measurements were performed. Note that if TEWL and/or skin hydration is to be quantified on different days for the same study participant, to the extent feasible, measurements should be made at the same time of day to minimize any possible effects of circadian rhythms.

2 Exogenous factors

a Hygiene (washing) practices prior to measurement, including conformance or deviations from instructions given to study participants.
b Use of any topical products, including conformance or deviations from instructions given to study participants. Note also if skin was dry wiped before measurement because of use of topical products.
c Exposure to chemicals or mechanical damage to the skin as a result of work.
d Use of any personal protective clothing or other materials that might have caused occlusion of the skin, including the type of covering, frequency, and duration of use, and time since last use.
e Ingestion of caffeinated beverages or smoking prior to measurement.

3 Environmental factors

a Calendar date, season, and time of TEWL and skin hydration measurements.
b Average outdoor ambient temperature and RH.
c Ambient workplace temperature and RH.



4 Experimental and measurement/instrumentation factors

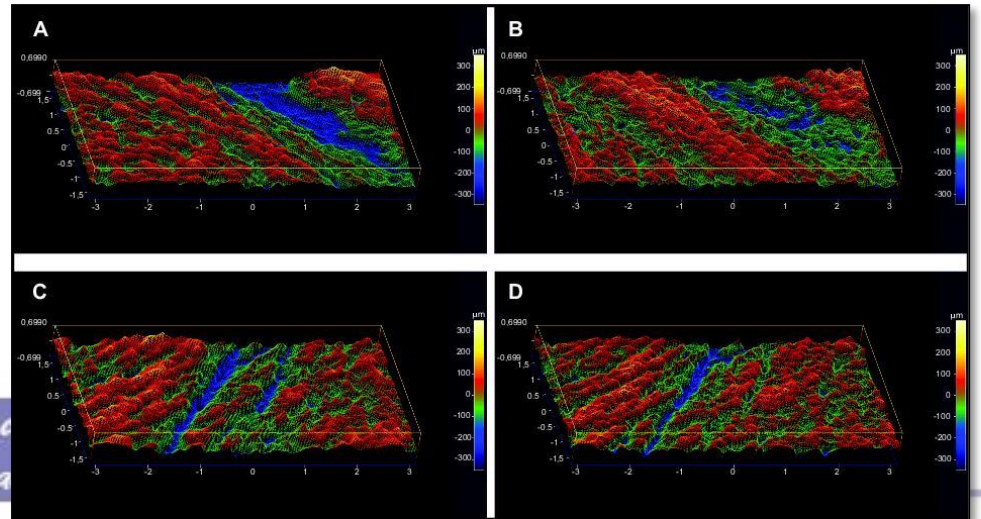
a The type of instrument/probe according to model and manufacturer.
b Equilibration time of TEWL instrument and/or hydration instrument in measurement environment.
c Calibration (manufacturer and prior to use, if applicable) of TEWL instrument and/or skin hydration instrument.
d Frequency with which the skin hydration probe calibration was verified during the study.
e Acclimatization conditions of study participants prior to measurements, including duration, ambient temperature, and RH in measurement area.
f How the instrument was applied to the skin surface, including handling of the TEWL probe and time to achieve a stable measurement in accordance with the manufacturer instructions.
g The number of measurements per anatomical position and lag time between measurements.





Najbolja praksa koja se primenjuje u eksperimentalnim studijama – *TDCC/Annex II*

- Posebni preduslovi za iznošenje tvrdnji **o uslovima pod kojima su testovi sprovedeni**:
- "*tolerance tested*„
- "*tested under medical supervision*„
- "*dermatologically tested*„
- "*clinically tested*".





"Tolerance tested"

- Tvrdnja "*ispitana/testirana podnošljivost*" znači da je proizvod podvrgnut testiranju pod nadzorom **naučno kvalifikovanog profesionalca** određenog da ispita njegovu podnošljivost **na ciljnoj grupi** i da rezultati ovih testova pokazuju da je proizvod dobro podnošljiv u ovoj grupi ispitanika.

Jedan od načina da se testira podnošljivost/neškodljivost



- **Dermatološko testiranje KP**

(*compatibility testing, patch test*)

Cilj testa je da se **proceni iritacioni potencijal na koži pod kontrolom dermatologa.**

Primenjuje se za procenu:

- Kozmetičkih sastojaka
- Smeša sastojaka
- Finalnih KP

"*Patch*" test preporučen je od SCCNFP/0068/98 kao značajno oruđe za procenu bezbednosti KP. "*Preporučuje se da se KP podvrgne ispitivanju kompatibilnosti sa kožom na prihvatljivom broju humanih ispitanika pre stavljanja na tržište/puštanja u promet*".

- ***Patch* test** ponovljenog izazivanja (***Human Repeated Insult Patch Test* - HRIPT**)

- Princip HRIPT-a: Studija ima za **cilj da se potvrdi kompatibilnost sa kožom i odsustvo alergenog potencijala KP nakon ponovljene primene na kožu** pod preuveličanim eksperimentalnim uslovima.

- Proizvod se primenjuje pod *patch*-em u toku definisanog vremena. Primena se ponavlja 9 puta u toku tri uzastopne nedelje, perioda neophodnog za moguću indukciju alergije. Posle najmanje 2 nedelje odmora, bez tretmana, proizvod se ponovo jednom nanosi na indukciono mesto na koži i na prethodno netretirano mesto i nakon definisanog vremena, postoje uslovi da se otkrije potencijalno indukovana alergija. Broj humanih dobrovoljaca je 50, starosti 18 -70 godina (muškarci/žene).

"Tested under medical supervision"

- Tvrdnja *"ispitano/testirano pod medicinskim nadzorom"* ukazuje da je **proizvod podvrgnut testovima sprovedenim pod nadzorom medicinski kvalifikovanih profesionalaca** kao što su doktor medicine ili stomatologije. Zavisno od predstavljanja tvrdnje, to se može, na primer, odnositi na specifičnu efikasnost proizvoda ili na podnošljivost na koži.

"Dermatologically tested"

- Tvrdnja *"dermatološki testirano"* nagoveštava da je proizvod testiran/ispitan na ljudima pod nadzorom dermatologa. Zavisno od predstavljanja tvrdnje može da se odnosi na specifičnu efikasnost ili podnošljivost proizvoda. Studije samo-percepcije od strane korisnika nisu pogodne da potkrepe takve tvrdnje.

"Clinically tested"

- Tvrdnja *"klinički testirano"* odnosi se na ekspertizu, postupak ili uslove pod kojima se sprovode testovi. *"Klinički testirano"* znači da je proizvod ispitan na ljudima pod nadzorom medicinski kvalifikovanih profesionalaca ili drugih naučno kvalifikovanih profesionalaca u skladu sa kliničkim protokolom ili u kliničkom ambijentu.

Kontrolisano kliničko ispitivanje

- Test performansi KP – spoljna percepcija

KP se ispituje u kontrolisanoj objektivnoj kliničkoj studiji, sa procenom od strane eksperta obučenog za procenu odabranih parametara. Rezultati ovog tipa ispitivanja klasifikuju se kao „objektivni“, sa jakim dokazom o ponovljivosti i saglasnosti između eksperata, ako ih je više.

- Test performansi KP – samo-procena

Proizvodi se testiraju u kontrolisanoj objektivnoj kliničkoj studiji, sa procenom od strane osoba koje samo-primenjuju KP i slede pre-definisana uputstva, a ocenjuju KP na skali koja je prethodno ustanovljena, ocenjujući intenzitet promene. Podaci koji se generišu klasifikuju se kao „subjektivni“.

Protokol studije - sadržaj

1. Cilj studije

2. Informacije o KP

- Tip proizvoda (npr. krem za kožu)
- KP koji treba da se ispita i referentni proizvod (ukoliko se koristi) uključujući identifikator proizvoda
- KP koji se testira treba da se lako identifikuje i sledi (serijski broj obavezan)
- Uslovi čuvanja KP i rok trajanja deklarisani/dati
- Količina KP koja treba da se primeni

3. Test procedura – opis

- Vremenski okvir – raspored merenja
- Mesto studije

Protokol studije - sadržaj

4) Primenjena metodologija i relevantni parametri

- Relevantnost metodologije za cilj studije
- Ključni test parametri
- Oprema koja će se koristiti
- Eksperimentalni dizajn uključujući broj uzoraka/broj testova/randomizaciju ispitivanja
- Procena parametara i merenja.

5) Dobrovoljci

- Kriterijumi za uključivanje i isključivanje: demografski, kriterijumi povezani sa studijom.
- Broj: opravdanje broja subjekata vezano za statističke ili druge metodološke ekspertize. Obično se uključuje više zbog odustajanja/izostavljanja iz različitih razloga.

Protokol studije - sadržaj

6) Procena parametara: definicija efikasnosti usvojenih parametara

7) Postupak primene KP

8) Hronologija ispitivanja, merenja

9) Upravljanje podacima – Procesovanje podataka – Analiza rezultata

Primeri studija koje su sprovođene na Katedri za FTK:
Istraživačke, pilot, komercijalne studije

Prva publikovana studija: 2004. godine,
Savić S. et al

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Vehicle-controlled effect of urea on normal and SLS-irritated skin

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Abstract

It is known that, depending on the concentration, treatment with urea could improve skin barrier function, despite its penetration-enhancing properties. This controversial skin effect of urea has been explored systematically in this study in terms of the effect of vehicle on the performance of urea. In the first part, a series of four semi-solid emulsions with 5% (w/w) urea, varying in the type of emulsion, nature of emulsifier and polarity of oil ingredients, have been evaluated with regard to their skin hydrating and transepidermal water loss (TEWL)-modifying properties. Placebo samples were tested alongside the urea-containing ones. Two best performing moisturisers from the above were chosen for the second part of the study, in which sodium lauryl sulphate (SLS)-irritated skin was treated with both placebo and urea-containing samples. In addition to TEWL and skin hydration level, the erythema index (EI) was measured before, during and after the treatment. The results have shown that barrier-improving and hydrating abilities of urea are bi-directional and dependent on both the type of vehicle used for its delivery and the state of skin.
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Keywords: Urea; Moisturiser; Skin hydration; TEWL; Erythema index; Emulsion

Protokol studije

The aim of the study was to evaluate long-term effects of daily use of four different types of emulsions, with and without urea as a moisturising agent, on both normal and SLS-irritated human skin. Skin parameters observed were TEWL, SC hydration level and erythema index (EI). The investigation was composed of two parts, both using double-blind randomised study design. In part I, the TEWL, electrical capacitance (EC) and sebum content (as a measure of any cream residue) on a flexor side of both forearms were evaluated. This was done on two groups of 15 volunteers during a 3-week treatment with the four test emulsions. In part II, the effects on barrier integrity, SC hydration level and erythema of SLS-irritated hand skin were evaluated in additional two groups of 10 volunteers, each treated for 5 days with two creams, chosen from part I.

2.3. Experimental design

In part I, 30 volunteers were divided in two groups (placebo and urea cream users), as reported in similar studies (Derde et al., 2000; Held et al., 2001):

Group 1 (15 volunteers, mean age: 24.2 ± 0.9): the flexor sides of both forearms were treated with the four placebo samples, using precisely delineated and marked cardboard ruler (with three empty spaces in the form of rectangles, each being 9 cm^2). Samples F1p and F2p were applied at the left, and F3p and F4p at the right forearm. At each forearm one rectangle was left as an untreated control.

Table 1
Composition of placebo emulsions (F2p–F4p); in active samples (F2a–F4a) 5% of purified water was replaced with urea

Ingredients/INCI	Sample % (w/w)		
	F2p	F3p	F4p
Oil phase			
Petrolatum	3.00	3.00	3.00
Mineral oil	3.00	3.00	3.00
Prunus dulcis	3.00	3.00	3.00
Isopropyl miristate	3.50	3.50	3.50
Caprylic/capric triglyceride	3.00	3.00	3.00
Coco-caprylate/caprate	4.00	4.00	4.00
Cetearyl alcohol	1.00		1.00
Polyglyceryl-4-isostearate		1.00	
Bees wax		1.20	
Hydrogenated castor oil		0.80	
Dimethicone	0.50	0.50	0.50
BHT, ascorbyl palmitate	0.05	0.05	0.05
Emulsifier			
Cetearyl glucoside (and) cetearyl alcohol	5.00		
Ceteareth-12			2.00
Ceteareth-20			2.00
Cetyl dimethicone copolyol		2.00	
Water phase			
Propylene glycol	3.00	3.00	3.00
Preservatives blend	0.50	0.50	0.50
Sodium chloride		0.5	
Aqua	70.45	70.95	71.45

Group 2 (15 volunteers, mean age: 22.6 ± 0.5): active creams with 5% urea in different vehicles (samples F1a–F4a) were applied in the same manner as placebo samples.

During part I of the study, subjects were treated for 21 days twice daily, in the morning and in the evening. TEWL, EC and sebum content were measured before their entry into the study (baselines), 30 min after the first application of the samples and then on days 7, 14 and 21, as well as 3 days upon the last application of the tested samples. Each measurement was carried out 10–15 h after previous treatment, i.e. the products were applied in the evening and the measurements were taken on the following day. The subjects were instructed to wash their arms normally and not to administer any product in the morning before the measurement. Based on the results of the first phase of the experiment, two emulsions were chosen for the part II of the study.

In part II, the skin on the back of the hand, previously exposed to 2% (w/w) SLS solution was treated (method outlined below). TEWL, EC, EI and sebum content were measured before the SLS exposure (baseline), 12–15 h upon the last immersion of the hand, and finally 12–15 h after the last application of the emulsions. The exposure of the skin of both hands to SLS solution was carried out 1 day after the baselines were taken, and was performed on 2 consecutive days. Following irritation, a 5-day long treatment with the two chosen creams was carried out. Participants were advised to wash their hands as usually.

Twenty volunteers that took part in this phase of the study were divided in two groups. Group 3 (10 individuals, mean age: 22.7 ± 0.8): dorsal side of the left hand was treated with the sample F2, using precisely delineated and marked cardboard ruler, so that the left half of the hand was treated with placebo and the right with urea-containing cream (each area 16 cm^2). The right hand served as an untreated control. Group 4 (10 individuals, mean age: 25.6 ± 3.6): treated with F3p and F3a in the same manner as group 3.

2.4. Sodium lauryl sulphate exposure

Experimental irritation was elicited by immersion of both hands into 2% (w/w) SLS solution (Ph.Eur.), warmed at 40 °C. Immersion took place for 10 min twice daily for 2 consecutive days, with an interval of at least 4 h between immersions (Ramsing and Agner, 1997; Fluhr et al., 2001).

2.5. Instrumental evaluation

All skin tests were performed after adaptation of participants to room conditions (30 min at 21 ± 1 °C and 45 ± 5% RH). The following order of measurements was performed: TEWL, EI (during part II of the study), skin capacitance and sebum content.

All measurements were carried out according to the relevant guidelines (Pinagoda et al., 1990; Fullerton et al., 1996; Berardesca, 1997; Rogiers, 2001).

TEWL was evaluated as an indicator of the skin barrier integrity using Tewameter TM 210. Electrical capacitance, indicating the hydration level of the outer epidermis, was measured by Corneometer CM 825 and the results presented in relative corneometer units (rcu). EI, as an indicator of the skin irritation,

Statistička analiza i neki rezultati

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was detected by Mexameter MX 18. Possible presence of the cream residue at the skin surface was checked by Sebumeter SM 810 (all instruments by Courage + Khazaka, Germany). An average of three measurements was used in all the cases, except for the EI (five readings).

2.6. Statistical analysis

The values of all observed parameters are given as means ± S.D.

In part I, following a positive testing for normality, parametric tests were used. Data involving values of parameters measured on forearm areas treated by different samples (F1 through F4, active and placebo, as well as the control site), at distinct time points, were analysed by the one-way within-subjects (repeated measures) ANOVA, followed by Tukey's *t*-test, where appropriate (Kuss and Diepgen, 1998; Fluhr et al., 2001). Differences between placebo and corresponding active cream-treated groups at distinct time points, were checked by Student's unpaired *t*-test.

In the second part of the study, due to inhomogeneity of the data, Friedman rank variance analysis with consecutive Dunn's comparisons was used to evaluate the statistical difference between the values of measured parameters (TEWL, EC, EI) at different time points (baseline, upon SLS irritation, and upon 5-day treatment), for each site (placebo, active treatment and control) separately. Differences between values obtained at the same time point, but for different regions of the tested hand skin (placebo versus active treatment versus control) were analysed by the one-way within-subjects (repeated measures) ANOVA followed by Tukey's *t*-test (Kuss and Diepgen, 1998; Fluhr et al., 2001).

$P < 0.05$ was considered significant for all test methods. Statistical analyses were performed with commercial statistical software Stat for Windows R. 5.0.

3. Results

All participants reported strict compliance with the instructions, including washing their arms in the morning prior to measurements. This was confirmed by the lack of the cream residue on the skin surface, measured by Sebumeter (absolute values being within the range 0–2 μg/cm², both at treated and control sites, as well as at each time point during the study).

3.1. Part I

The results of the first part of the study are presented in Tables 2 and 3and Figs. 1–4. Table 2 summarises the means for TEWL after treatments with placebo (group 1, samples F1p–F4p) and active (group 2, samples F1a–F4a) samples and presents the significance levels between samples, mutually and related to untreated control. In the same manner, Table 3 sums up the results for EC of placebo and urea-containing creams. In addition, graphical representation of percentage change related to corresponding control value for each emulsion type (F1–F4) are shown in Figs. 1–4 (*t*-test, $P < 0.05$).

Table 2
TEWL (g/m²/h) of placebo samples (F1p through Fp4) and active samples (F1a through F4a), with corresponding control values, during the test period; results are given as means ± S.D.[a]

Sample	Time (min/day)					
	Baseline	30 min	7 days	14 days	21 days	3 days upon treatment
F1p left	8.6 ± 2.1	8.1 ± 2.9	7.5 ± 1.2[3,4]	6.6 ± 1.2[4]	5.9 ± 1.6[4]	5.5 ± 1.5[3,4]
F2p left	7.3 ± 1.3	7.8 ± 2.5	10.3 ± 3.9*[1,3]	7.9 ± 1.4*	6.4 ± 1.6[4]	6.6 ± 1.[3,4]
F3p right	7.1 ± 2.0	6.1 ± 1.3	7.2 ± 1.4[3,4]	6.6 ± 1.2[4]	7.2 ± 1.7[4]	6.8 ± 1.7[1,4]
F4p right	8.7 ± 2.5	8.2 ± 1.6	10.9 ± 2.5*[1,3]	9.8 ± 2.9*[1,2,3]	10.2 ± 3.2*[1,2,3]	9.5 ± 1.3*[1,2,3]
Control left	7.4 ± 2.1	7.7 ± 2.3	7.8 ± 1.3	7.1 ± 1.9	6.6 ± 1.7	6.7 ± 1.3
Control right	7.7 ± 1.9	7.8 ± 1.8	8.1 ± 2.4	6.8 ± 1.7	6.3 ± 1.8	5.9 ± 1.5
F1a left	7.3 ± 2.4	8.3 ± 3.0	9.9 ± 2.6*[3,4]	6.7 ± 1.8[4]	6.5 ± 2.4[2,3,4]	7.8 ± 1.9*[2,3,4]
F2a left	6.5 ± 1.3	7.6 ± 1.7	9.6 ± 2.1*	6.6 ± 1.2[4]	5.2 ± 2.0*[1]	5.7 ± 2.0[1]
F3a right	7.7 ± 2.3	6.7 ± 1.9	8.6 ± 2.9[1]	4.7 ± 2.3 *[1,2,4]	5.2 ± 1.8*[1]	5.7 ± 1.3[1]
F4a right	7.3 ± 2.1	6.2 ± 2.0	8.3 ± 2.1[1]	5.8 ± 1.9[1,2,3]	5.3 ± 1.8*[1]	6.5 ± 1.9[1]
Control left	7.5 ± 1.8	7.1 ± 2.3	7.5 ± 1.7	6.1 ± 1.9	6.5 ± 2.4	6.1 ± 2.1
Control right	7.8 ± 2.2	7.5 ± 1.9	7.9 ± 3.0	5.9 ± 2.0	6.4 ± 2.7	6.3 ± 1.9

[a] On the given time point (baseline, 30 min, 7, 14, 21, 3 days upon treatment withdrawal), significant group differences ($P < 0.05$) according to Tukey's post hoc analysis were given related to corresponding control values (*), or to values obtained under treatments with samples F1p through F4p, i.e. F1a through F4a (numbers 1 through 4 in superscript, respectively).

Table 3
Electrical capacitance (EC, rcu) of placebo samples (F1p through F4p) and active samples (F1a through F4a), with corresponding control values, during the test period; results are given as means ± S.D.[a]

Sample	Time (min/day)					
	Baseline	30 min	7 days	14 days	21 days	3 days upon treatment
F1p left	29.4 ± 3.7	35.9 ± 5.2*	37.8 ± 4.1*[2,3,4]	36.5 ± 4.5*[2]	33.7 ± 3.7*[2]	30.7 ± 3.4*[2]
F2p left	27.4 ± 2.8	35.5 ± 3.9*	45.5 ± 3.1*[1,3,4]	46.1 ± 3.2*[,1,3,4]	44.4 ± 3.9*[1,3,4]	36.6 ± 3.8*[1,3,4]
F3p right	27.1 ± 2.9	32.3 ± 3.2*	33.9 ± 3.0*[1,2]	33.7 ± 4.0*[2]	30.9 ± 2.6*[2]	29.4 ± 2.7*[2]
F4p right	26.4 ± 2.6	33.5 ± 2.5*	33.9 ± 3.5*[1,2]	32.5 ± 3.2*[2]	29.6 ± 3.2*[2]	29.3 ± 3.3*[2]
Control left	25.8 ± 2.4	27.3 ± 2.1	24.7 ± 3.1	23.3 ± 2.7	23.2 ± 2.5	22.6 ± 2.2
Control right	27.0 ± 2.6	26.9 ± 4.1	25.9 ± 2.7	22.7 ± 3.5	22.5 ± 3.8	22.7 ± 2.7
F1a left	26.1 ± 5.0	30.3 ± 2.9*	36.0 ± 3.1*	33.0 ± 3.0*[4]	35.5 ± 3.1*[3,4]	30.1 ± 3.2*
F2a left	27.4 ± 2.8	33.1 ± 3.2*	38.8 ± 2.8*	33.9 ± 2.8*[4]	35.7 ± 2.9*[3,4]	31.7 ± 2.2*
F3a right	24.7 ± 2.8	24.4 ± 2.3	38.8 ± 3.0*	33.2 ± 2.8*[4]	38.5 ± 3.2*[1,2,4]	31.9 ± 2.8*
F4a right	25.0 ± 2.4	29.8 ± 2.7*	37.5 ± 3.2*	26.7 ± 1.8[1,2,3]	32.2 ± 2.1*[1,2,3]	29.6 ± 2.4*
Control left	24.7 ± 2.1	24.9 ± 2.4	24.2 ± 3.1	23.5 ± 3.2	23.1 ± 2.7	22.5 ± 2.7
Control right	25.3 ± 2.8	26.9 ± 3.1	26.9 ± 2.7	23.3 ± 3.0	22.3 ± 2.7	22.0 ± 2.7

[a] The same as Table 2.

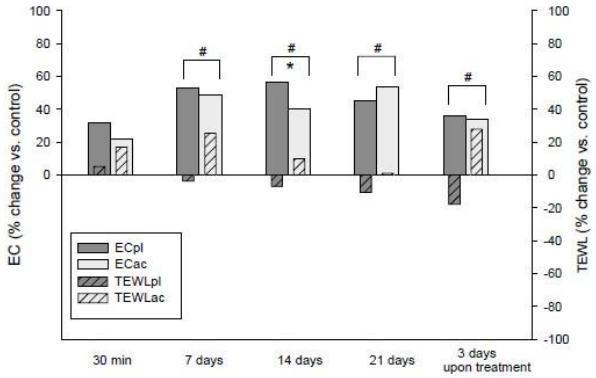


Fig. 1. The effect of topical application of sample F1 (Cold cream) ($n = 15$) without urea (F1p, dark grey bars) and with 5% urea (F1a, light grey bars) on EC (open bars—wider) and TEWL (hatched bars—narrower), related to control (percent change). Differences between placebo and active cream-treated groups at distinct time points were checked by Student's unpaired *t*-test, significant differences ($P < 0.05$) being marked with (#) for TEWL, and with (*) for EC.

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Primer II: ispitivanje efekata/efikasnosti preparata za samotamnjenje kože (*self-tanning*)

- Preparat u fazi razvoja finalne formulacije

  Sastav: Ingredients/INCI – Aqua, Coco-Caprylate/Caprate, Dicaprylyl Ether, Dixydroxyacetone (DHA)/Erythrulose, Glyceryl Stearate, Cetearyl Alcohol, Glycerin, Ceteareth-20, Cetyl Palmitate, Ceteareth-12, Tocopheryl Acetate, Dimethicone, Preservatives, Parfum

  Uzorak 1 – 3% DHA; Uzorak 2 – 3% DHA + 2% eritruloze;

  Uzorak 3 – 5% DHA

CILJEVI

- odabir proizvoda sa optimalnim efektom samo-tamnjenja i povoljnim uticajem na barijernu funkciju kože
- procena režima primene (količina/učestalost)

KONCEPT: GO – NO GO

Eksperimentalni dizajn

- Ispitanici: n=11 (ženski pol, 23.36±1.63 god., bez vidljivih znakova patoloških promena na koži)
- Volarna strana desne i leve podlaktice
- Tretirana površina – 16 cm^2 po uzorku + netretirana kontrola
- Količina nanetog uzorka: 0.02 g/cm^2 – dva nanošenja u razmaku od 24h
- Isključeni svi ostali tretmani dva dana pre i tokom testiranja
- Ambijentalni uslovi: RH - 50±5% i T – 20 ±1°C

Merenja:

1) bazalni status
2) 24h posle I primene
3) 24h posle II primene

Procena efekata:

- Instrumentalne tehnike
- Self-assessment

Instrumentalne tehnike/statistička analiza

- Melanin indeks (Mexameter® MX 18, Courage+Khazaka, Nemačka) – apsolutne razlike u odnosu na bazalnu vrednost
- Vlažnost kože/SC – (rcu, Corneometer® CM 825)
- Transepidermalni gubitak vlage (TEWL, g/cm^2/h, Tewameter® TM 210)
- Direktna "image" analiza

❖Student t-test za zavisne uzorke

❖Analiza varijanse za ponovljena merenja, post-hoc Tukey test


Skin-pH-meter
PH 900
Sebumeter
SM 810
Corneometer
CM 825

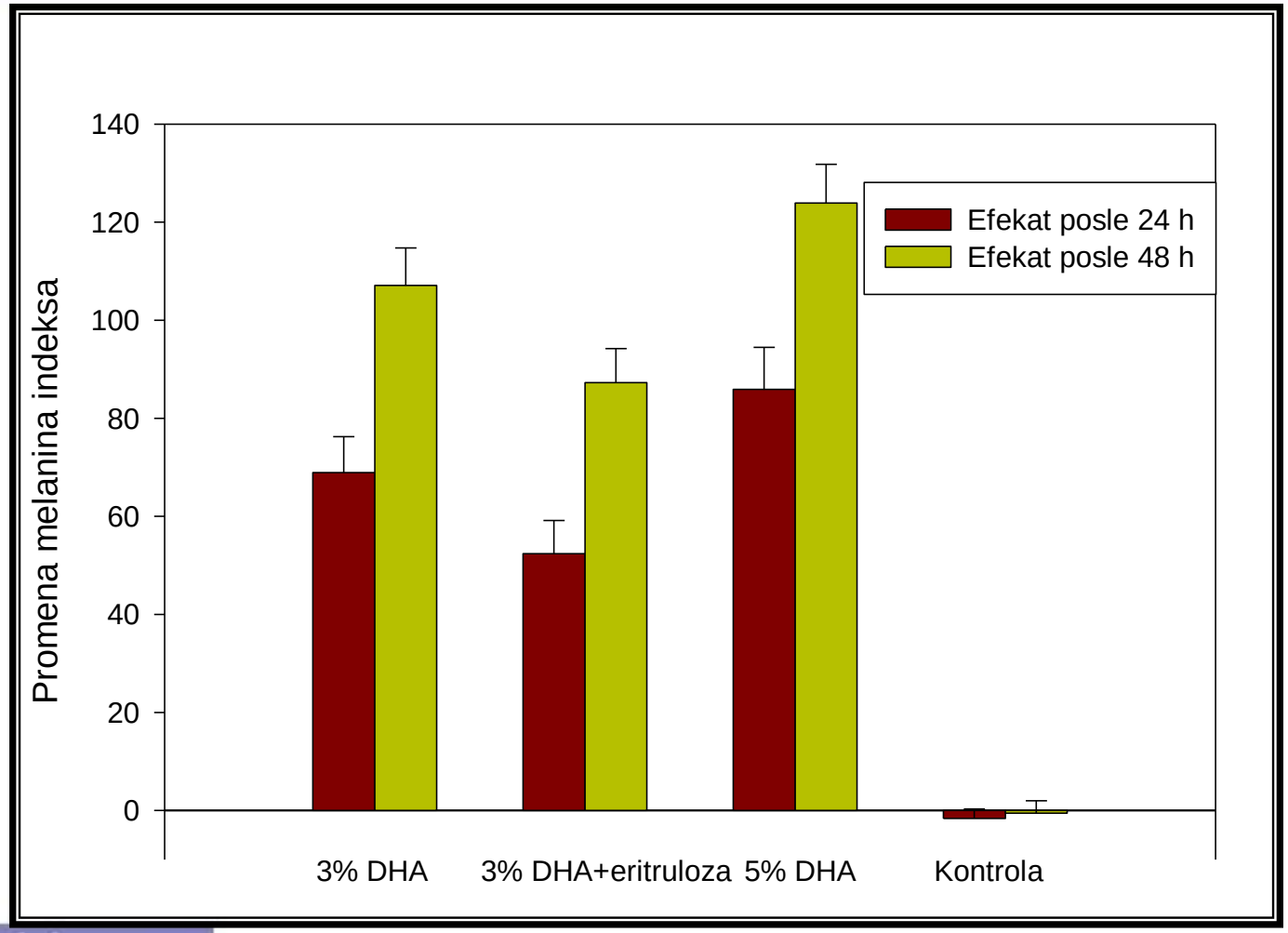

Mexameter®
MX 18


Tewameter TM 210

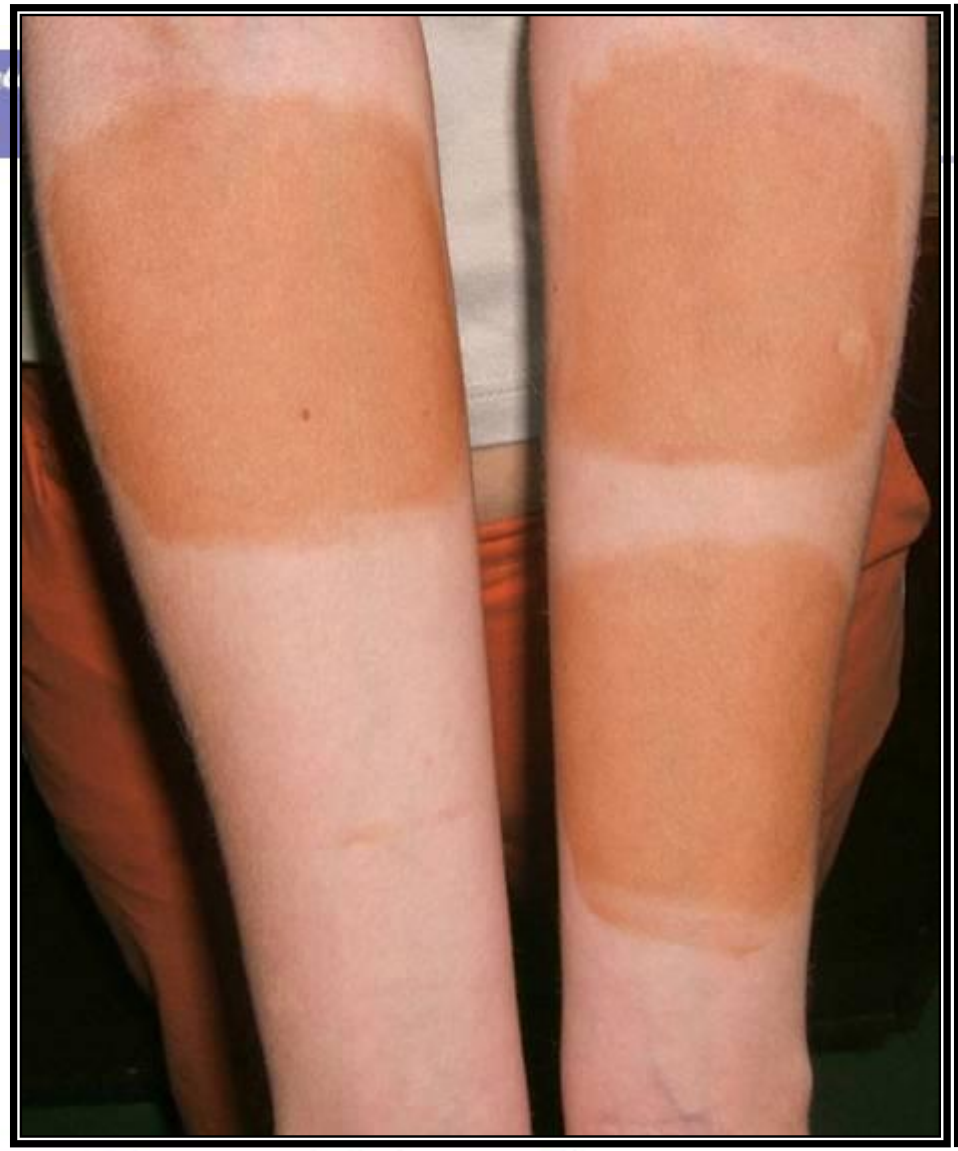

Tewameter TM 210


Mexameter®

Uticaj ispitivanih uzoraka na promene melanin indeksa

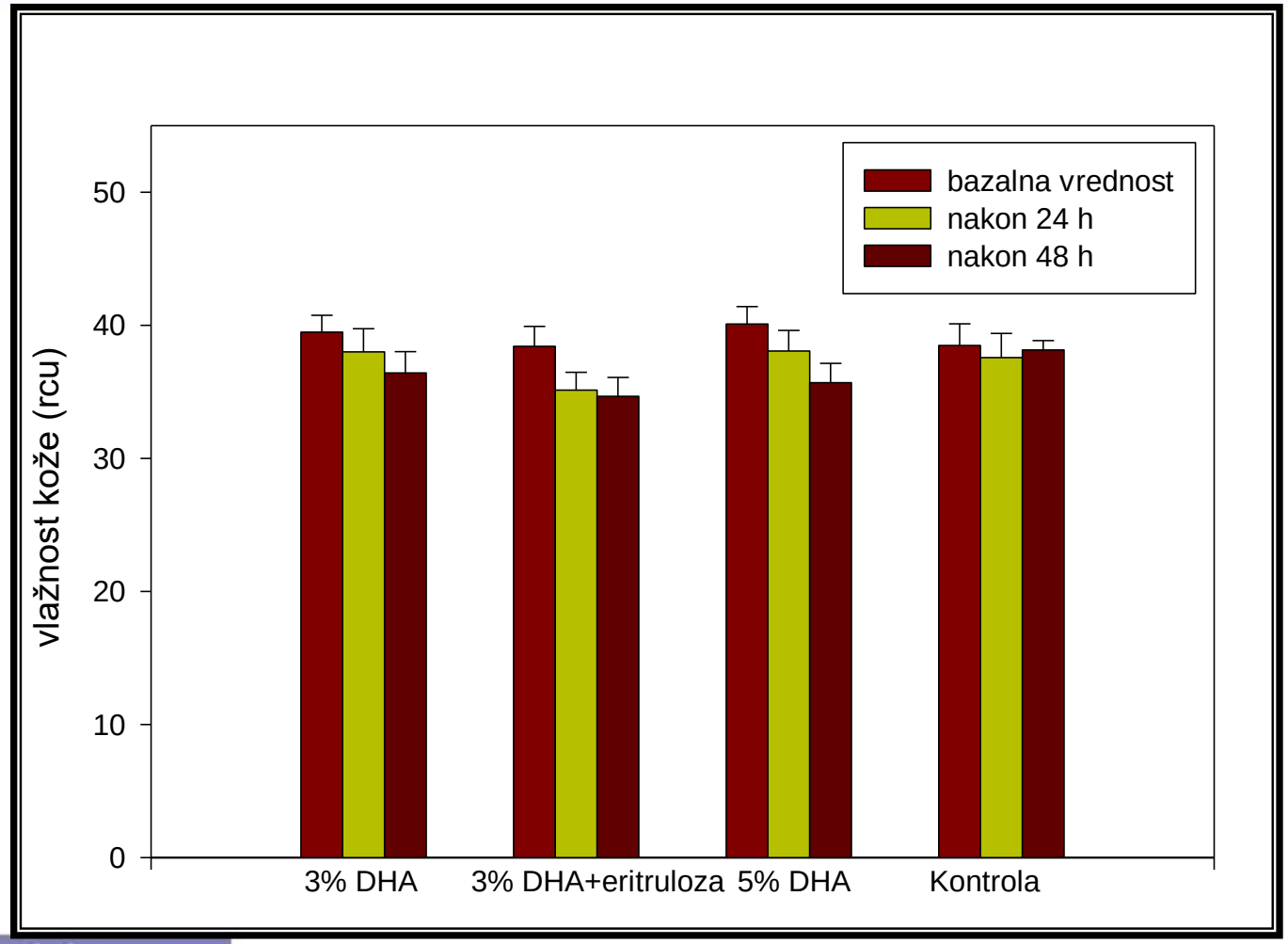




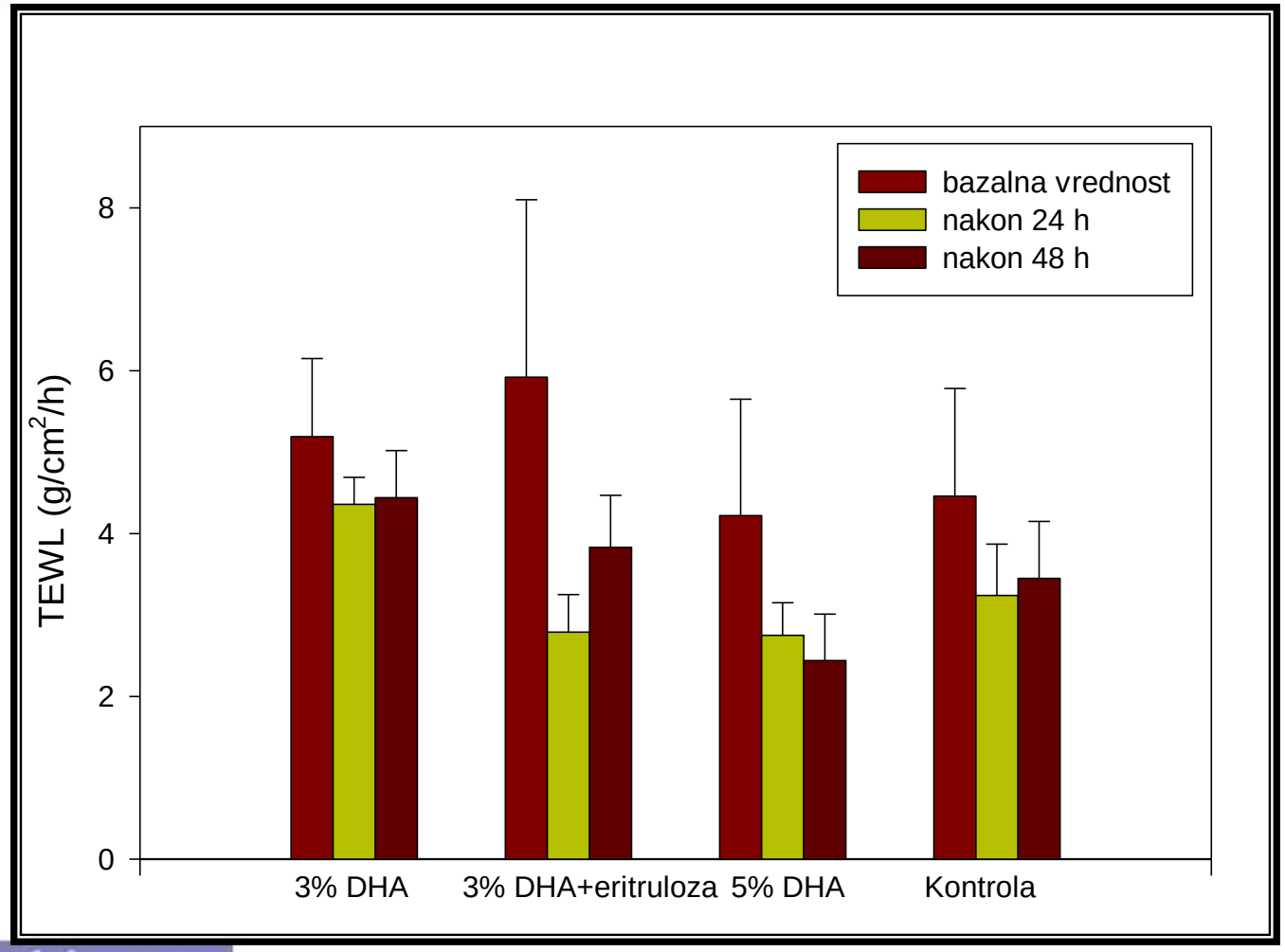




Uticaj ispitivanih uzoraka na vlažnost kože



Uticaj ispitivanih uzoraka na TEWL



Zaključak studije

- Optimalni efekat samotamnjenja proizveo je uzorak 1 sa 3% DHA (najpovoljniji skor objektivna/subjektivna procena)
- Izostanak negativnih efekata DHA na vlažnost kože
- Očuvana barijerna funkcija kože
- Ponovljena primena statistički značajno povećava efekat samo-tamnjenja
  - **Za ujednačenost i ton boje važni količina i način nanošenja preparata**

ADEKVATNO UPUTSTVO ZA PRIMENU I INFORMISANOST KORISNIKA

Otkrivena tajna lepote Kejt Midlton? Studiju o "prirodnom botoksu" koji koristi vodili srpski naučnici

Princeza od Velsa očigledno voli da održava svoju mladolikost na sasvim prirodan način



Šta je u osnovi najpopularnijeg gela na svetu?

Gel se oslanja na ***spilantol, lokalni anestetik ekstrahovan iz biljke parakresa - Acmella oleracea***.

Potencijalni benefiti spilantola dovode se u vezu sa njegovim glavnim aktivnim molekulom N-alkilamid-spilantolom.

Prema studiji objavljenoj u International Journal of Cosmetic Science, spilantol brzo opušta mišiće slično botoksu, stvarajući „primetno smanjenje“ finih linija i nabora, prenosi "Cosmeticsdesign.com".

„U studiji o serumima sa ekstraktom Acmella oleracea, koju su vodili srpski naučnici, navodi se da bore mogu da se ublaže u roku od dve nedelje, ističući sigurnost proizvoda.“

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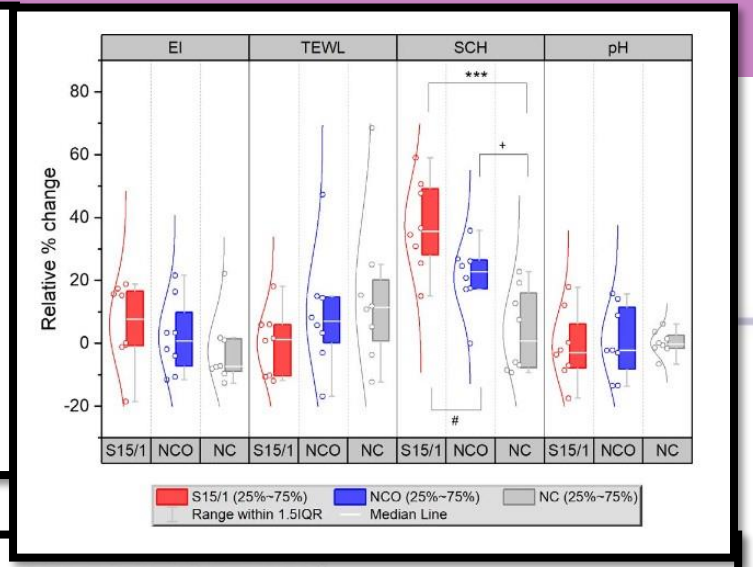
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International Journal of Cosmetic Science
SOCIÉTÉ FRANÇAISE DE COSMÉTOLOGIE

ORIGINAL ARTICLE

'All-natural' anti-wrinkle emulsion serum with *Acmella oleracea* extract: A design of experiments (DoE) formulation approach, rheology and *in vivo* skin performance/efficacy evaluation

Sanela M. Savic[1] | Nebojsa D. Cekic[1,2] | Sasa R. Savic[2] | Tanja M. Ilic[3] | Snezana D. Savic[3]



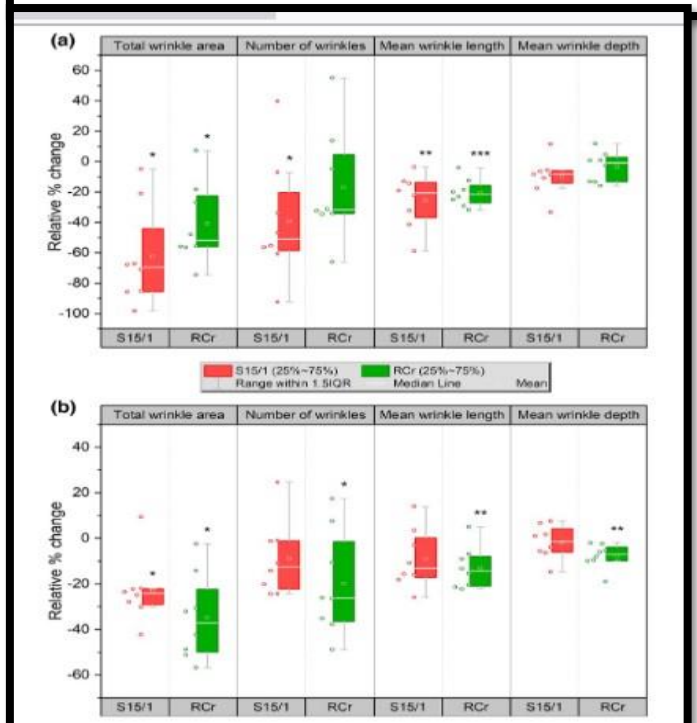


FIGURE 4 *In vivo* efficacy study of the developed *Acmella oleracea* extract-containing natural anti-wrinkle serum: relative percentage changes in the skin wrinkle parameters from baseline to 2 weeks of application of the tested serum (S15/1) and reference cream (RCr) in the periorbital (a) and perioral (b) areas of human volunteers. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, for parameter values 2 weeks after product application compared to corresponding basal values (paired *t*-test, Wilcoxon test) [Colour figure can be viewed at wileyonlinelibrary.com]

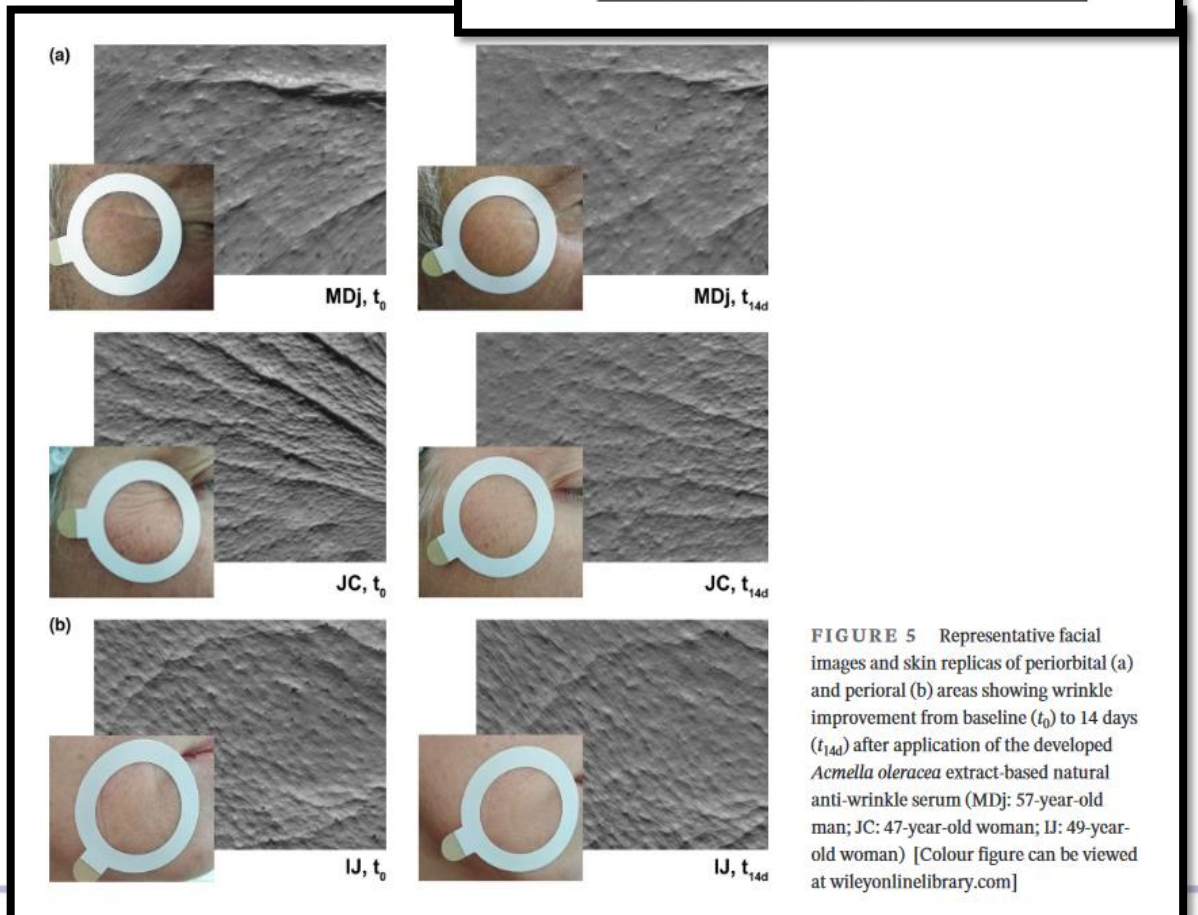


FIGURE 5 Representative facial images and skin replicas of periorbital (a) and perioral (b) areas showing wrinkle improvement from baseline (t_0) to 14 days (t_{14d}) after application of the developed *Acmella oleracea* extract-based natural anti-wrinkle serum (MDj: 57-year-old man; JC: 47-year-old woman; IJ: 49-year-old woman) [Colour figure can be viewed at wileyonlinelibrary.com]

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International Journal of Cosmetic Science

ORIGINAL ARTICLE

Formulation of topical acidic products and acidification of the skin – Contribution of glycolic acid

Milica Lukic[1] | Mila Filipovic[2] | Nevena Pajic[1] | Dominique Lunter[3] | Dragana Bozic[4] | Snezana Savic[1]

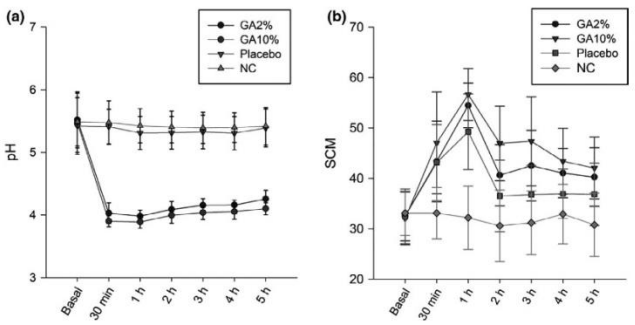


FIGURE 5 (a) pH (mean value ± standard deviation) and (b) stratum corneum moisturization (SCM) at different time points prior (Basal) and after (30 min, 1, 2, 3, 4 and 5 h) investigated creams (Placebo, GA2% and GA10%) application with corresponding non-treated control (NC) results

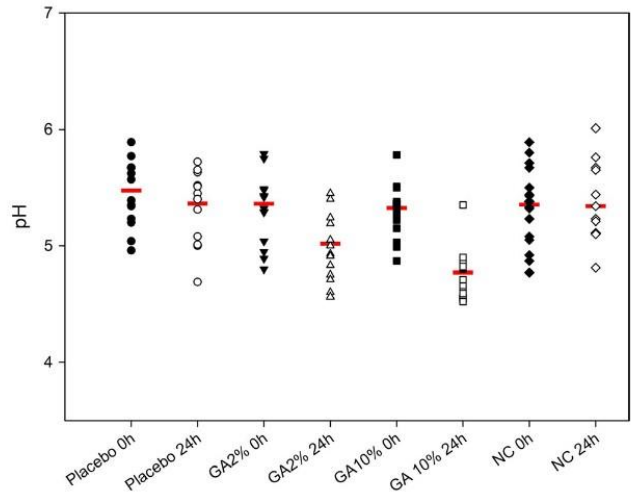


FIGURE 6 All pH values at different time points prior (0 h) and 24 h after investigated creams (Placebo, GA2% and GA10%) application with corresponding non-treated control (NC) results; red dash represents mean value

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Topically applied lipid-containing emulsions based on PEGylated emulsifiers: Formulation, characterization, and evaluation of their impact on skin properties ex vivo and in vivo

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pharmaceutics
MDPI

Article

Efficient Development of Green Emulsifier/Emollient-Based Emulsion Vehicles: From RSM Optimal Experimental Design to Abridged In Vivo Assessment

Mila Vukašinović [1], Sanela Savić [2,3], Nebojša Cekić [2,3], Tanja Ilić [1], Ivana Pantelić [1,*] and Snežana D. Savić [1]

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ETIČNOST!

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Član 8.

Komitet u okviru svoje delatnosti obavlja sledeće poslove:

. Procenjuje primenu etičkih principa povezanih sa različitim vrstama biomedicinskih istraživanja koja se rade na Fakultetu, odnosno u okviru projekata čiji je nosilac ili učesnik Fakultet i sa istraživanjima koje organizuje i izvodi Fakultet a u kojima učestvuje nastavno osoblje Fakultета, odnosno studenti poslediplomskih studija. Pod biomedicinskim

istraživanjima podrazumevaju se: kliničка ispitivanja lekova, medicinskih sredstava i kozmetičkih proizvoda; epidemiološka anketna i dijetarna istraživanja, kao i biohemijska, toksikološka i genetička ispitivanja biološkog materijala humanog porekla, ispitivanja zbirki pretходno sakupljenog biološkog materijala (uzorci tkiva i telesnih tečnosti) za koje nije potrebna saglasnost ispitanika.

1. važanost protokola predloženog kliničkog istraživanja (cilj istraživanja, naučnu zasnovanost tj. mogućnost da se zaključci donesu na najmanjem mogućem broju ispitanika uz prihvatljiv rizik i opravdanost predviđenog rizika i neugodnosti u odnosu na očekivani terapijski doprinos)
2. kompetentnost odgovornih istraživača za predložena istraživanja (kvalifikacije, usavršavanje, iskustvo), njihovih saradnika i podobnost ustanove u kojoj se istraživanje obavlja (opremljenost). Komitet razmatra kvalifikacije istraživača i njihovih saradnika na osnovu najnovijih biografija
3. ispravnost i potpunost pisanih informacija koje se daju ispitaniku ili njegovom zakonskom zastupniku
4. način na koji se obavlja izbor ispitanika, kako se informišu učesnici ispitivanja i kako se dobija pristanak ispitanika da učestvuju u studiji
5. osiguranje ispitanika kojim se od mogućег rizika u vezi sa istraživanjem obezbeđuju ispitanik i istraživač
6. predlog o tome na koji način će se lečiti ispitanik, odnosno na koji način će mu se osigurati nadoknada u slučaju oštećenja zdravlja ili smrti, ako je takav ishod direktno povezan sa ispitivanjem
7. izdatke za istraživanja, uključujući i predviđene naknade ispitanicima
8 finansijsku kompenzaciju ispitanicima ukoliko je to predviđeno (iznose i načine plaćanja) i druga pitanja vezana za informisanost ispitanika.

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HVALA NA PAŽNJI!