Skin and Formulation, 6th Symposium
Current challenges in skin formulation

ABSTRACT BOOK

2&3 Octobre 2023 Nantes, France

ABOUT US

WHO WE ARE

APGI – Association De Pharmacie Galénique Industrielle or
International Society for Drug Delivery Sciences and Technology

The APGI was founded in 1964 to promote activities and facilitate professional exchanges in Pharmaceutics, Biopharmaceutics, Pharmaceutical Technology and related fields. Everybody (students, academics, industrials, regulators, etc.) who is working in these areas is warmly welcome. While we are a French association, we are proud to have members from all aover the world (e.g., more than 50% are living outside France).

WHAT WE DO

The APGI organizes a variety of events, including Information Days, Workshops, Hot Topic Days as well as different National and International Scientific conferences.

Visit our website: www.apgi.org and join us, start your membership today and benefit from free Information Days, significant discounts on scientific congresses and symposia, and networking with individuals sharing the same passion about Pharmaceutical Technologies.

INDEX

APGI

Association Pharmaceutique Galénique Industrielle (International Society for Drug Delivery Sciences and Technology)
3 rue du Professeur Laguesse
59000 Lille

Opening Hours

Sunday, 1 october	14:30 - 18:00
Monday, 2 october	08:00 - 17:30
Tuesday, 3 october	08:15 - 17:30

Venue

La cité des Congrès/ Nantes
5 rue de Valmy
44041 Nantes Cédex 01

PUBLIC TRANSPORT

Tramway : Line 1 - « Duchesse Anne - Château des Ducs de Bretagne » station, juste one stop from the TGV train station (north exit)

Busway : Line 4 - « Cité Internationale des Congrès » stop.

For more information : www.tan.fr/en

CHAIRS AND COMMITTEES

Chairs of the Conference

Prof. Vincent Faivre, Paris-Saclay University
Dr Anne-Marie Pensé-Lhéritier (HDR), President of FRMGalesens

Organizing committee members

Dr Frédéric Bonté, Director of Scientific Communication, Guerlain
Prof. Laurence Coiffard, Nantes University
Prof. Vincent Faivre, Paris-Saclay University
Prof. Nicolas Huang, Paris-Saclay University
Dr Valérie Muguet, Project Manager, Galenic Formulation, Laboratoires Pierre Fabre, Division Medical Care
Dr Anne-Marie Pensé-Lhéritier (HDR), President of FRMGalesens

SOCIAL PROGRAMME

The coktail reception will be held on

Monday, 2 October 2023
From 19:30 — 23h

And will take place at the «Machines de l'Ile», a unique artistic universel on the site of the former Nantes shipyards

SCIENTIFIC PROGRAMME

MONDAY 2 OCTOBER 2023

08:00 Registration and welcome coffee

09:00 Welcome introduction

OPENING LECTURE

09:15 **Prof. Marc Brown, Medpharm - UK**
Risk mitigation in Topical Product Development: Orthodoxy, Automation and Innovation

SKIN BIOLOGY AND PATHOLOGIES

10:00 **Prof. Laurent Misery, University of Brest - France**
Sensitive skins: diagnosis and management

10:35 Tbc

10:55 Posters session & exhibition – coffee break

11:25 **Dr Georgios Stamatas, Johnson & Johnson Santé Beauté - France**
Recent advances in skin maturation during infancy and childhood

12:00 **Dr Catarina Rosado, Universidade Lusofona - Portugal**
Lipid-based nanocarriers based on insect biomass to tackle atopic dermatitis

12:20 **Simran Chaurasia, PhD Student, Maharaja Ranjit Singh Punjab Technical University - India**
Design and development of Nano-carrier Based Bilayer Therapeutic System for Ungual Drug Delivery

12:40 Posters session & exhibition – lunch break

NEW DIRECTION IN SKIN DELIVERY: FORMULATION

14:00 **Xavier Ormancey, Laboratoires Pierre Fabre - France**
« Controversial » excipients: strategy on substitution depending on regulatory status

14:35 **Dr Laurianne Simon, University of Montpellier - France**
Lypopolyoxazolines nanoformulations for improved skin delivery

14:55 **Mathis Benyaya, PhD Student, University of Lyon - France**
Co-encapsulation of several actives in Pickering emulsions for topical delivery application

15:15 **Hishda Mohamed, SEDERMA - France**
Several carrier systems to increase the benefits of active substances

15:35 Posters session & exhibition – coffee break

16:15 **Dr François-Xavier Legrand, University Paris-Saclay – France & Prof. Emilie Munnier, Facutly of Pharmacy of Tours – France**
Deep Eutectic solvents for skin formulations

17:00 **Christoph Heuberger, Lipoïd - Switzerland**
Effects of Phospholipids on Skin Retention and Penetration

19:30 Cocktail reception

SCIENTIFIC PROGRAMME
TUESDAY 3 OCTOBER 2023

08:15 | Door opening

STRATEGIES OF FORMULATION

08:45 | **Dr Joana Marques Marto, University of Lisbon - Portugal**
Waterless formulation in skin research

09:20 | **Dr Melanie Köllmer, RADES - Germany**
Preservation of topical formulation: requirements and strategies

09:55 | **Prof. Guoping Lian, University of Surrey - UK**
An end-to-end in-silico simulation workflow to understanding the formulation effect on perrcutaneous absorption

10:15 | **Posters session & exhibition** – coffee break

10:45 | **Dr Pascale Gauthier, Auvergne University - France**
Packaging as a full partner for protect formulations

11:20 | **Lara Gorsek, PhD student, University of Barcelone - Spain**
Biomechanical properties of Sepigel with Flurbiprofen loaded Nanoparticles in vivo

11:40 | **Benjamin Gavinet, Seppic - France**
Topical formulation of high concentration of cationic-form lidocaine hydrochloride with anionic rheology modifiers

12:00 | **Yvonne Wiedemann, PhD student, University of Tuebingen - Germany**
Poly(vinyl alcohol) Based Cryogel Patches as Drug Delivery Systems for Topical Application

12:20 | **Posters session & exhibition** – lunch break

NEW DIRECTION IN SKIN DELIVERY: TECHNOLOGIES

13:45 | **Dr Morgan Dos Santos, LabSkin Creations - France**
Advances and Innovations of 3D Bioprinting Skin for the Performance Evaluation of Cosmetic Products

14:20 | **Prof. Ryan Donnelly, Queen's University Belfast - UK**
Micro-needles and skin applications, new developments

14:55 | **Paraskevi Kyriaki Monou, PhD Student, University of Thessaloniki - Greece**
Fabrication of 3D printed coated microneedles with electrosprayed containing rivastigmine and N-acetyl cysteine nanoparticles for combined transdermal delivery

15:15 | **Dr Franciska Erdö, Pazmany Peter Catholic University - Hungary**
Raman spectroscopy in skin research

15:50 | **Lucas Chiarentin, PhD Student, University of Coimbra - Portugal**
Towards the development and optimization of a rheology method for a high viscosity cream: An Analytical Quality by Design (AQbD) approach

16:10 | **Dr Katy Margulis, The Hebrew University of Jerusalem - Israël**
Mass-Spectrometry Imaging-Guided Design of Dermal Delivery Systems

16:30 | **Conclusion**

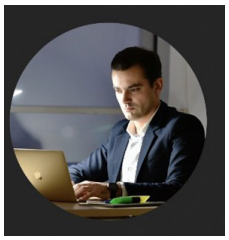
INVITED SPEAKERS

Prof. Marc Brown BSc PhD, CChem FRSC

Prof. Marc Brown co-founded MedPharm in August 1999 and he has been the guiding force behind MedPharm's scientific developments and intellectual property since its inception. He currently acts as Board Director and Chair of MedPharm's Scientific Advisory Committee. Prior to MedPharm he was an academic in the Pharmacy Departments at King's College London (KCL) and the University of Hertfordshire. He retains honorary and visiting Professorships at the University of Reading, KCL, and De Montford University and in 2022 was awarded the status of Professor Emeritus of the University of Hertfordshire. He has over 200 publications and 26 patents describing his work. His research interests lie mainly in drug delivery to the skin, nail and airways and to date, he has been involved in the pharmaceutical development of over 55 products that are now on the market in Europe, America and Japan.

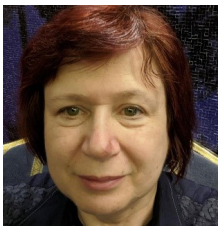
Prof. Ryan Donnelly, Queen's University Belfast

Professor Ryan Donnelly holds the Chair in Pharmaceutical Technology at Queen's University Belfast and is Director of QUB's interdisciplinary research programme Materials & Advanced Technologies for Healthcare (MATCH). His personal research is centred on design and physicochemical characterisation of advanced polymeric drug delivery systems for transdermal and intradermal drug delivery, with a strong emphasis on improving patient outcomes. He is currently developing a range of novel microneedle technologies through independent research, but also in collaboration with several major pharma partners. He has obtained substantial UK Research Council, charity and industrial funding and authored over 600 peer-reviewed publications (H-index = 76), including 6 patent applications, 6 textbooks, 23 book chapters and approximately 300 full papers. He has been an invited speaker at numerous national and international conferences. Professor Donnelly is Europe/Africa Editor of Drug Delivery & Translational Research and a member of the Editorial Board of the Journal of Controlled Release. He has won Visit Belfast's Ambassador Award for Life & Health Sciences (2022), the Academy of Pharmaceutical Science's Innovative Science Award (2020), the Controlled Release Society's Young Investigator Award (2016), BBSRC Innovator of the Year (2013), the American Association of Pharmaceutical Scientists Pharmaceutical Research Meritorious Manuscript Award (2013 & 2022), the GSK Emerging Scientist Award (2012) and the Royal Pharmaceutical Society's Science Award (2011).



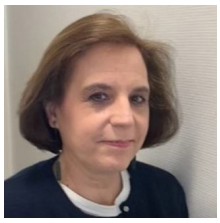
Dr Morgan Dos Santos, PhD, General Manager and Chief Scientific Officer of LabSkin Creations

Morgan DOS SANTOS is currently General Manager and Chief Scientific Officer of LabSkin Creations, a biotech company specialized in advanced tissue engineering and dedicated to the testing of cosmetics and pharmaceutical products on in vitro skin models.With a PhD in molecular and Cellular biology from Lyon University, France, Morgan has been developing for the past 20 years a high expertise in skin tissue engineering and 3D bioprinting. Originally trained in Edouard Herriot Hospital, one the the largest burn repair centre in Europe, he then moved to the cosmetics industry in which he actively contributed to the development of disruptive innovations in the field of skin bioengineering and skin care actives for dermatological and cosmetics applications. After 7 years in China, working on skin fundamental research to transform disruptive science into innovation and new cosmetics product adapted to Asian consumers, he co-founded 2 biotech startup companies in the field of personal care testing and regenerative medicine, LabSkin Creations and HealShape. Morgan is author or co-author of many peer-reviewed journal papers and book chapters in the fields of tissue engineering and regenerative medicine, and he is also the co-inventor of PCT patents in bioprinting, epigenetics and active ingredients.



Prof. Franciska Erdo, PhD, Faculty of Information Technology and Bionics, Pazmany Peter Catholic University

Dr Franciska Erdő has a PhD degree in pharmacy and pharmacology. She was working for research institutes in Germany (Max Planck Institute for Neurological Research, Cologne and Charité University, Berlin) and in Hungary (BIOREX Ltd, Veszprém and IVAX Drug Research Institute, Budapest) for several years. She has experience also from pharmaceutical industry (Sanofi-Synthelabo-Chinoin and SOLVO Biotechnology). Her previous projects focussed on the analysis of pathophysiology of stroke, blood-brain barrier and development new therapeutic strategies. Since 2014 she has been working for Pázmány Péter Catholic University, Budapest as an associate professor and as a labhead. She moved to dermatology and cosmeto-scientific research fields. Her main expertise is drug delivery across the physiological barriers (dermal barrier, nasal barrier, blood-brain barrier etc.). Currently she is involved in a collaborative research on skin analysis and RAMAN spectroscopy with University of Tours, France. Also she is the supervisor of PhD, MSc and BSc students. She is the author of more than 70 scientific papers and several book chapters and editor of books.



Dr Pascale Gauthier, Pharmacist, PhD, Charge of courses, Clermont-Auvergne University

Pascale Gauthier is a Pharmacist (D. Pharm.) with a research background: Biopharmaceutical Master (DEU) 'New gelling process for oils, study of manufacture of sun care oleogels', specific Master in Pharmacokinetic (DEA) 'Pharmacokinetic study of antihypertensive drug and its metabolites after single and repeated dose' and PhD 'Rotogranulation process used for manufacture of spheres.' She was involved in several patents, international publications, conferences, Thesis and is judging for Pharmapack Awards (Exhibitors and Health products categories), CPhI (Excellence in Pharma various) and Design French Institute (Janus). Her researches focus on modified release forms, pharmaceutical design and categories of users, digital in health and beauty areas as well as innovative packaging and formulations for drug forms and cosmetics.

Dr Melanie Köllmer, Co-Founder and Head of Formulation Development, RaDes

Dr Melanie Köllmer is head of formulation development at RaDes. She has more than 10 years of experience in pharmaceutical and biomedical research. Her expertise lies in the implementation of development projects, from formulation design of semi-solid dosage forms in feasibility studies to clinical phase and process development. She studied pharmacy at Philipps-University in Marburg, Germany, and received her PhD in drug delivery and tissue engineering from the University of Illinois at Chicago, USA, in the laboratory of Prof. Dr Richard A. Gemeinhart, followed by a PostDoc at the Illinois Institute of Technology (IIT) in Prof. Dr Eric Brey's laboratory. Subsequently, Melanie worked as a formulation scientist at Almirall Hermal. In close cooperation with analytical development as well as drug discovery, the IP and Regulatory Affairs departments, she worked extensively on the design of semi-solid formulations and the evaluation of new topical excipients and technology platforms. In particular, she made decisive contributions to the successful development of a stable aqueous tacrolimus cream (Patent WO2019233722). She focuses on rational design, cosmetic optimization, and characterization of semi-solid formulations for small molecules and probiotics. A special focus is the use of modern rheological methods to optimize stability, manufacturing processes and user friendliness of formulations. Melanie Köllmer is the author of currently nine publications in the field of drug delivery and in vitro performance testing and regularly gives presentations in the field of formulation development and rheology.

Dr François-Xavier Legrand, Associate Professor, Paris-Saclay University

François-Xavier LEGRAND was born in Béthune (France) in 1984. He completed a Ph.D in Organic and Macromolecular Chemistry at the University of Artois in November 2010. He then obtained a Post-Doctoral Engineer-Researcher position in the Laboratory of Structure and Dynamics by NMR at the French Alternative Energies and Atomic Energy Commission in Saclay. In September 2011, he was appointed Associate Professor at Paris-Saclay University (formerly Paris-Sud) and joined the team Multiscale Physical Chemistry for Pharmaceutical Sciences (formerly Physico-Chemistry of Multiphasic Systems) at the Institut Galien Paris-Saclay. His current work is focused on the design and the characterization of complex supramolecular systems based on cyclodextrins and / or lipids with or without molecules of interest for drug delivery, especially for the treatment of acute myeloid leukemia. Since 2018, he has been interested in the effect of deep eutectic solvents on the skin for pharmaceutical and cosmetic applications as well as their use for the cutaneous delivery of therapeutic molecules. In this context, he was awarded a young researcher grant from the French National Agency for Research in 2019 to study the use of deep eutectic solvents for the treatment of cutaneous leishmaniasis. More recently, he has also focused on better understanding the behaviour of deep eutectic solvents after oral administration.

Dr Joana Marques Marto, PhD, Assistant Professor at Faculty of Pharmacy, University of Lisbon

Joana Marques Marto is currently an Assistant Professor at Faculty of Pharmacy, University of Lisbon. Since the beginning of her career, Joana Marto's main research interests have been the development and characterization of drug delivery systems for topical application. Further, she always focused on transposing the fundamental research to the applied (market).

Prof. Laurent Misery, University of Brest

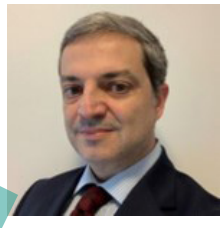
Professor of dermatology at the university of Brest, head of the department of dermatology of the university hospital of Brest, director of the french expert centre on pruritus, director of the laboratory interactions neurons-keratinocytes (LINK), chair holder of the partnership chair of neuro-sensory dermatology, author of more than 50 referenced papers on sensitive skin.

Prof. Emilie Munnier, Faculty of Pharmacy of Tours

Emilie Munnier is a professor at the Faculty of Pharmacy of Tours where she has been teaching pharmaceutical technology and cosmetology for more than 10 years. She is also a researcher in the team EA6295 NMNS Nanomedicines and nanoprobes. After her Pharm degree, she obtained a PhD in Life and Health Sciences at the University of Tours dealing with nanotechnologies for health. Using her skills in formulation and analytical chemistry, she currently focuses on innovative formulation, among which the encapsulation of active molecules to improve their penetration into the skin, but also to control their interaction with the ingredients of a finished pharmaceutical or cosmetic product. She is also interested in the development of bioanalytical methods to measure the stability and the efficacy of cosmetic products. She has been coordinator of several research projects involving actors of the cosmetic industry, and is currently coordinating the ANR project DES4Skin dealing with the use of natural deep eutectic solvent (NaDES) as innovative ingredients for cosmetic products.

Xavier Ormancey, MSc, Laboratoires Pierre Fabre

Mr. Xavier Ormancey, MSc, is the Director of Research and Development for Pierre Fabre Dermo-Cosmetics and Personal Care. He has more than 35 years experience in the beauty industry in France and in USA (L'Oréal, Chanel, Yves Rocher, Beautycounter). As a specialist of natural cosmetics and clean beauty, he initiated the Conscious Care inception at Pierre Fabre, which enables the formulation of a new generation of dermo-cosmetic products safer and more efficient but also more committed and more respectful of resources and people.



Dr Georgios Stamatas, PhD, Research Associate Director & Fellow, Translational Science, Johnson & Johnson Consumer Health

Dr Georgios Stamatas is a Research Associate Director and Fellow, in Essential Health Translational Science at Johnson & Johnson. His research focuses on method development and applications on understanding skin physiology and topical product effects. His work on the differences between pediatric and adult skin and has transformed our understanding of newborn and baby skin maturation. Dr. Stamatas holds a PhD in Chemical/Biomedical Engineering from Rice University and has co-authored more than 100 scientific publications and patents.

POSTER SESSION

1. **Design and Optimization of Liposomes Containing Ceramide to Restore Skin Barrier by Expetimental Design**
   Humeyra Sahin Bektay, Ali Asram Sagiroglu, Kubra Bozali, Eray Metin Guler, Sevgi Güngör
2. **Formulation of shea butter-based lipid nanoparticles for topical and transdermal applications**
   Carmen F.W. Kabore, B. Gérard Josias Yameogo, Denis Wouessidjewe, B. Charles Sombie, Hermine Zime Diawara, Rasmané Semdé, Annabelle Gèze
3. **Impact of different phospholipid-based emulsifiers on physical stability of topical multiphase systems and their effects on cell viability**
   Katja Steiner, Victoria Klang
4. **Influence of iontophoresis on transdermal delivery of ketoprofen loaded deformable liposomes into the synovial fluid: In vitro and in vivo evaluation**
   Vanaja Kenchappa, S. Salwa, HN Shivakumar, SN Murthy
5. **Liposomal encapsulation and release to protect and treat the skin**
   Adria Botet-Carreras, Oscar Domenech, Mireia Mallandrich, Ana C. Calpena-Campany, M. Teresa Montero, Jordi H.Borrell
6. **Liposome-based dissolving microneedles loaded with rifampicin for improved treatment of MRSA-induced skin infection**
   Qonita Kurnia Anjani, Anjali K. Pandya, Sara Demartis, Juan Dominguez-Robles, Natalia Moreno-Castellanos, Huanhuan Li, Elisabetta Gavini, Vandana B. Patravale, Ryan F.Donnelly
7. **Nanostructured Lipid Carriers as a Protective Nanoreservoir of Hyperforin in St. John's Wort Extract: Preliminary Studies**
   Yoana Sotirova, Iliyan Kolev, Velichka Andonova
8. **Transfersomes for cutaneous and lymphatic targeting of Rose Bengal to treat melanoma**
   Sara Demartis, Qonita Anjani, Giovanna Rassu, Paolo Giunchedi, Aaron Hutton, Akmal Sabri, Ryan F.Donnelly, Elisabetta Gavini
9. **Bi-gel: an innovative topical dosage form. A case study with Lavandula angustifolia essential oil**
   Delphine Pelisson, Wendy Monteiro, Elise Dauphin-Chanard
10. **Borage Oil-Based Bigels for Topical Delivery of Nanoencapsulated St. John's Wort Extract: Textural and Rheological Characterization**
    Velichka Andonova, Yoana Sotirova, Krastena Nikolova
11. **Development and Characterization of Calcitriol Loaded In-Situ Gel for Enhancing Orthodontic Tooth Movement**
    Nitasha Chauhan, Amit Bhatia
12. **Effect of Poloxamer 407 / Borago oil bigel containing methanol extract of St. John's wort loaded nanostructured lipid carriers in skin wound application on blood liver and kidney damage**
    Velichka Andonova, Yoana Kiselova-Kaneva, Oskan Tasinov, Stefka Stoeva, Minka Hristova
13. **Formulation and in vitro premeation evaluation of NSAID Drug microemulgel**
    Sarah Bouameur, Soumia Chirani
14. **Study of the biomechanical properties of a hydrogel loaded with pranoprofen lipid nanoparticles**
    Negar Ahmadi, Mireia Mallandrich, Ana Calpena, Maria Rincon
15. **Three-dimensional scaffolds of chitosan with antibacterial properties for skin tissue engineering applications.**
    Ioanna Koumentakou, Zoé Terzopoulou, Anna Michopoulou, Dimitrios Bikiaris

16. **Topical delivery of metronidazole using a green-crosslinked gelatin-based hydrogel sheet-mask for the treatment of PPE-related skin-lesions**
Angelica Graça, Sara Raposo, Helena Margarida Ribeiro, Joana Marto

17. **«Ex vivo» Transdermal Study on Human Skin of a Baricitinib Microemulsion**
Roya Mohammadi Mey Abadi, Nuria Garros, Marc Soriano, Mireia Mallandrich

18. **Co-encapsulation of several actives in Pickering emulsions for topical delivery application**
Mathis Benyaya, Yves Chevalier, Marie-Alexandrine Bolzinger, Claire Bordes

19. **Cosmetic Pickering emulsions stabilized by natural source of protein-based particles**
Magalie Cabannes, Amandine Rousset, Jean-Yves Berthon

20. **Development of a crisaborole nanoemulsion for the treatment of atopic dermatitis**
Lupe Carolina Espinoza, Paulo Sarango-Granda, Lilian Sosa, Maria Rincon, Ana Calpena, Mireia Mallandrich

21. **Development of a micro-emulsion containing cannabidiol for topical use: a pre-formulation study**
Teresa Areses-Huete, Damian Cordoba-Diaz, Ana I. Torres-Suarez, Manuel Cordoba-Diaz

22. **Ex-vivo skin retention and permeation of crisaborole from innovative topical formulations**
Cristina Padula, Sara Nicoli, S. Pescina, Patrizia Santi

23. **Eye irritation potential of red raspberry seed oil after nanoemulsification: assessment with the HET-CAM test**
Ana Gledovic, Tanja Ilic, Ivana Pantelic, Snezana Savic

24. **Formulation of a microemulsion containing cannabidiol and an extract from S. ebulus for potential anti-inflammatory use**
Teresa Areses-Huete, Damian Cordoba-Diaz, Manuel Cordoba-Diaz

25. **Formulation of Innovative O/W Emulsions Containing Curcumin Derivatives with Enhanced Antioxidant Capacity for Skin Application**
Nikolaos Bikiaris, Dalla Evdokia, Ioanna Boumentakou, Nikolaos Nikolaidis

26. **Formulation, Characterization and Evaluation of Innovative O/W Emulsions Containing Curcumin Derivatives with Enhanced Antioxidant Properties**
Evangelia Balla, Evdokia Dalla, Ioanna Koumentakou, Nikolaos Bikiaris, Smaro Likidou, Nikolaos Nikolaidis

27. **Innovative Skin Product Emulsions with Enhanced Antioxidant, and UV Protection Properties Containing Nanoparticles of Chitosan with Encapsulated Tannin**
Dimitrios N.Bikiaris, Victoria Gavriliadou, Ioanna Koumentakou, Nikolaos Nikolaidis

28. **Pickering emulsions stabilized by quercetin for topical applications: influence of oil properties**
Blandine Boche, Soukaina Benoujja, Nicolas Huang, Bertrand Fournier

29. **Advanced rheological characterization of topical products: an accurate tool to discriminate and optimize formulations**
Manon Rossano, Delphine Pelisson, Jacob Yu, Philippe Caisse

30. **Alpha-tomatine: a promising natural ingredient for skin care formulations**
Catarina Faria-Silva, Denise Scavone, Joana Marto, Pedro Simoes, Manuela Carvalheiro, Sandra Simoes

31. **Are makeup products sources of PFAs in Europe?**
Céline Couteau, Catherine Brunet, Laurence Coiffard

32. **Ceramides as the cornerstone in simple and advanced formulations targeted at renewal of disrupted skin barrier**
Aneta Kalvodova, B.Bozena Michniak-Kohn, Jarmila Zbytovska

33. **Changes in Skin Barrier Properties Associated with Exposure to Surfactant and Alcohol Cleansers**
Denise Li Ngay Ying, David Moore, Daniel Hodgson, Sara Brown, Wilson Poon

34. **Contribution of ethanol extracts from wheat, corn and sunflower waste material to the properties and effects of cosmetic products**
Ana Ciric, Dragana Bozic, Mila Filipovic, Milika Lukic

35. **Dermal compatibility and improved barrier function of a new octenidine and silver citrate-based emollient for atopic-prone skin**
José M.Gairi, Anna Castany, Isabel Fernandez

36. **Effect of topically applied bolalipid surfactants PC-C24-PC and PC-C32-PC on corneocyte cohesion**
Namarig Adbelrahman, Lea Ann Dailey, Victoria Klang

37. **Exploring a Possible Relationship between Transepidermal Water Loss and Ceramide Levels in Porcine Stratum Corneum**
Moritz Reuter, Hans Schoenfelder, Dominique Jasmin Lunter

38. **Impact of emollients on release studies from O/W creams**
Maria Elvira Franco Gil, Joana Marto, Helena Margarida Ribeiro

39. **Neutral natural deep eutectic as anti-biofilm agents in skin formulations**
Helene Liepelt Nistedt, Krister Gjestvang Gronlien, Rebekka Rekkedal Rolfsnes, Hanne Cecilie Winther-Larsen, Ole Andreas Loche Okstad, Hanne Hjorth Tonnesen

40. **New molecules as SPF boosters**
Giulia Signori, Cecilia Anselmi, Marisanna Centini, Alessandro Sega, Stefano Gianni

41. **Optimization of ORAC assay combined with in vivo tape stripping for the assessment of antioxidant efficacy of cosmetics formulations**
Tanja Ilic, Ana Gledovic, Vladimir Dobricic, Ivana Pantelic, Snezana Savic

42. **Phycocyanin-enriched Cosmetic Gels: NaDES as Stability Enhancers?**
Iron Mike Ardeza, Soukaina Hilali, Laura Wils, Xavier Perse, Emilie Munnier, Leslie Boudesocque-Delaye

43. **Skin permeation enhancement effect by tartaric acid - meglumine ionic liquid system**
Takayuki Furuishi, Sara Taguchi, Kaori Fukuzawa, Etsuo Yonemochi

44. **Study of the potential antioxidant activity of lupin beans' by-products for cosmetic and pharmaceutical applications: a green extraction approach**
Aline Caramona, Joana Duarte, Joao Seixas, Joana Marto

45. **Sustainable Cosmetics: Harnessing the Potential of Natural Deep Eutectic Solvents for Cream Formulation**
Alexis Verger, Roxane Grard, Iron Mike Ardeza, Xavier Perse, Salima Bouderbala, Céleste De Graef, Alexandra Despres, Leslie Boudesocque-Delay, Emilie Munnier

46. **Thermal Water combined with Thymus x citriodorus hydrolate as core ingredients of anti-aging cosmetic products**
Ana Rita Gama, José Martinez-de-Oliveira, Ana Palmeira-de-Oliveira, Rita Palmera-de-Oliveira

47. **Waste materials from Wheat, Corn and Sunflower in cosmetic products**
Ana Ciric, Milika Lukic

48. **3D Printing: new directions to personalize the delivery of (bio)actives from topical patches**
Sara Bom, Pedro Pinto, Helena Margarida Ribeiro, Joana Marto

49. **A Combined approach to better understand the absorption perception of skincare products**
Beatriz Arruda Valença, Ecaterina Gore

50. **Application of physiologically based pharmacokinetic modelling to predict the in vitro dermal permeation of the UV filter octocrylene**
Yanling Zhang, C.Krishna Telaprolu, James Clarke, Sebastian Polak, Yuri Dancik

51. **Bioprinting technology to build a new equivalent skin model with sebaceous gland-like structures**
Alba Cico, Vanessa Bergeron, Catherine Vandermee, Mikael Garcia, Caroline Ringenbach, Bruno Brisson, Fabien Guillemot, Philippe Mondon

52. **Characterization of knee aging by fringes projection, standardized pictures and viscoelastic methods**
Emmanuel Doridot, Emilie Pinard, Marion Leonard, Céline Bondil, Philippe Mondon

53. **Dermatological analysis of allergic contact dermatitis and psoriasiform dermatitis in mouse models**
Dorottya Kocsis, Hiche Kichou, Fabiola Kreis, Kende Lorincz, Barnabas Banfi, Emilie Munnier, Roland Csepanyi-Komi, Franciska Erdö

54. **Hydrogel-forming microneedles with solid dispersion reservoirs for the long-acting transdermal delivery of atorvastatin**
Yara A.Naser, Ismaeil A.Tekko, Lalitkumar Vora, Ke Peng, Helen O.McCarthy, Ryan F.Donnelly

55. **In Vitro Permeation Testing: Assessment of Sampling Techniques and Analytical Methods**
Leanne Page, Frank Toner, Cheryl Liu, Ashvin Patel, Bruna Lousada

56. **Investigation of the suitability of confocal Raman spectroscopy for the demonstration of bioequivalence of topical products**
Annette Gaiser, Dominique Jasmin Lunter

57. **Low field NMR methods to evaluate the hydration state of skin explants**
Magali Martin Biran, Scott Laroche, Sylvie Laurent

58. **Microfluidic manufacture of highly loaded melatonin snedds using 3D printed chips for treatment of vesicant chemical warfare agents effects**
Baris Ongoren, Dolores R.Serrano, Juan Torrado, Aytug Kara, Aikaterini Lalatsa

59. **Optimization of iontophoresis protocol for the skin penetration of a charged hydrophilic cosmetic active**
Tiffanie Sala, Claire Bordes, Baptiste Bonnemaire, Marie-Alexandrine Bolzinger

60. **Progress in thermodynamic modelling of formulation effect on percutaneous absorption**
Guoping Lian, Nicola Piasentin, Tao Chen, Qiong Cai

61. **Systematic investigation of sorbitan esters applied on ex-vivo porcine skin analyzed by trans-epidermal water loss (TEWL) and confocal Raman spectroscopy (CRS)**
Hans Schoenfelder, Moritz Reuter, Dominique Jasmin Lunter

62. **Tactile Sensory Evaluation: an essential tool to evaluate skin-product interaction**
Ecaterina Gore, Céline Picard, Géraldine Savary

63. **Understanding the evaporation of the fragrances from the skin**
Elise Hadjiefstathiou, Daria Terescenco, Catherine Malhiac, Céline Picard, Géraldine Savary

64. **X-ray diffraction - A sensitive tool for assessing collagen quality in cosmetic tests**
Jean Doucet, Emilie Leccia

65. **DuPontTM LiveoTM silicone topical excipients addressing drug delivery performance challenges for skin disorders management**
Virginie Caprasse, Iryacinthe Henin, Hyder Aliyar, Teresa Gorski

66. **DuPontTM LiveoTM toolbox of innovative silicone resin blends and film forming formulations for topical indications**
Virginie Caprasse, Iryacinthe Henin

67. **Nanoparticulate systems for dermal delivery of antimycotics**
Damla Orhan, Josef Beranek, Jarmila Zbytovska

68. **Optimization of Protein loaded PVP/VA dissolvable microneedle array by using Design of Experiment (DOE) approach**
Laura Koenitz, Abina Crean, Sonja Vucen

69. **PCL patches with antimicrobial surfaces for wound healing applications**
Nikolaos Bikiaris, Ioanna Boumentakou, Zoi Terzopoulou, Nikolaos Kehagias

70. **Synthesis and characterization of hemostatic patch based on chitosan with enhanced antibacterial activity.**
Ionna Koumentakou, Despoina Meimaroglou, Dimitrios N.Bikiaris

71. **Synthesis and characterization of poly (butylene succinate) nanoparticles loaded with heparin for hemostatic applications**
Rizos Bikiaris, Ioanna Koumentakou, Desmina Meimaroglou, George Z. Kyzas

72. **Therapeutic strategies for the management of hair loss: the role of pharmaceutical technology**
Jacopo Forte, Maria Gioia Fabiano, Federica Rinaldi, Gemma Caro, Alfredo Rossi, Carlotta Marianecci, Maria Carafa

73. **Transdermal human skin permeation study of a nanoparticle containing a derivate flavanone from natural resources**
Berenice Andrade-Carrera, Ma.Luisa Carduno-Ramirez, Ana Calpena-Campany, Paola Bustos-Salgado

74. **Curcumin Nanomicelles for the topical treatment of melanoma**
Silvia Tampucci, Valentina Paganini, Susi Burgalassi, Patrizia Chetoni, Daniela Monti

75. **Dermal Delivery of Phytochemicals: Storage Stability of Mono- and Multiphase Systems with Panax Ginseng Extract and Skin Permeation Ex Vivo**
T. Pfleger, EM. Schweiger, Z. Dekic, S. Strohmaier, VI Walter, A. Tahir, V. Klang

76. **Evaluation of the transdermal absorption of Olive oil-based formulations loaded with baricitinib for the treatment of Alopecia Areata**
Negar Beirampour, Ana Cristina Calpena, Maria Nuria, Valeri Dominguez, Mireia Mallandrich

77. **Formulation of a 2-in-1 shampoo based on Cocos nucifera oil (Arecaeae) for the prevention of traction alopecia in black women**
Ismael Dally Laba, Awa Tuo, Anne Marie Tanoh, Sandrine Aka Any-Grah, A. N'Guessan, José Arthur Lia Gnahore, Clémence N'Guessan

78. **Anti-stretch marks cosmetics : actives and formulations among marketed products**
Julia Pinheiro, Ana Palmeira-de-Oliveira, Diana Esteves, Rita Palmeira-de-Oliveira

79. **Artemether and lumefantrine dissolving microneedle patches with improved pharmacokinetic and efficacy for uncomplicated malaria caused by Plasmodium falciparum**
Fabiana Volpe-Zanutto, Leticia Tiburcio Ferreira, Fabio Maranhão T. Costa, Mary Ann Foglio, Ryan F. Donnelly

DESIGN AND OPTIMIZATION OF LIPOSOMES CONTAINING CERAMIDE TO RESTORE SKIN BARRIER BY EXPERIMENTAL DESIGN

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There is an impairment of skin integrity derived from derangement of orthorhombic lateral organization caused by dysregulation of ceramide (CER) amounts in the skin barrier. The impaired skin barrier is replenished via CER, fatty acid, and cholesterol-containing nano-based formulations. However, it is still a challenge to formulate CER-containing-liposomes due to their chemical structure with poor aqueous solubility and high molecular weight. In this study, the design and optimization of CER-NP loaded liposomes are implemented by Response Surface Methodology (RSM) based on the quality-by-design approach. The formulation optimization process of liposomes containing CER-NP was carried out using the Design of Expert. The Central Composite Design was the design type with 3 factors at 5 levels: plus and minus alpha (axial points), plus and minus (factorial points), and the center point. The parameters were CER-NP, fatty acid, and cholesterol at 5 variable levels as independent variables. The responses were the particle size and PDI values of liposomes as responses which were measured using dynamic light scattering (DLS). The optimum formulation was selected based on mean particle size (136.6 ±4.05) and PDI values (0.248 ±0.012), and the prediction model success was evaluated based on the equation on the quadratic model. The encapsulation efficiency was clarified by sampling the CER-NP-loaded liposome with the centrifugal ultrafiltration method and analysis in high-performance liquid chromatography (HPLC). The Cer-NP release from liposome was examined based on the in vitro release (IVRT). MTT assay was also performed on HaCaT human keratinocyte cell lines to assess the relative safety of the optimized liposomes loaded CER-NP. The experimental result (PS:136.6±4.05 nm and PDI: 0.248 ±0.012) and predicted result (PS:132.6 nm and PDI:0.278) were correlated. The CLSM image was conformable with the other studies and the encapsulation efficiency of CER-NP was 93.84±0.87%. The release profile was fitted with the Korsmeyer-Peppas model. The cytotoxicity studies showed that the liposomes for topical administration of CER-NP could be considered relatively safe. In conclusion, the optimized liposomes containing CER-NP could have the potential to restore the skin barrier function.

Keywords: Ceramide, liposome, skin barrier function, experimental design, topical administration

FORMULATION OF SHEA BUTTER-BASED LIPID NANOPARTICLES FOR TOPICAL AND TRANSDERMAL APPLICATIONS

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Shea butter is a natural lipid widely used in topical formulations because of its hydrating, anti-inflammatory and regenerative properties on the skin. Due to its non-irritant and nontoxic properties, it is safe to use in skin damages [1,2]. The aims of this study was to develop lipid-based nanoparticles using local shea butter as building material for topical and transdermal applications. The nanoparticles of shea butter were made using three different processes (high shear homogenization [3], phase inversion temperature [4] or solvent injection techniques [5]. The formulation factors optimized were the concentration of the shea butter introduced (1-30 mg/mL), the nature and the proportion of the solvent used, the presence of surfactant and the final volume of the preparation after evaporation. The obtained nanoparticle suspensions were evaluated for particle size using dynamic light scattering, polydispersity index, zeta potential and physicochemical stability. Subsequently the aqueous colloidal suspension obtained by high shear homogenization technique was converted into a gel by adding 0,5 % Carbopol 980NF (polymer) as a gelling agent and subsequent neutralization with sodium hydroxide. The gel formulations were investigated for pH and viscosity measurements at day 0. The viscosity was assessed at 26°C using a rotational viscometer STS-2011 (shear rate of 2 s-1, spindle n°R4, 10 rpm). The size of the nanoparticles was increased with an increase of the shea butter content in the three manufacturing process used. The optimized conditions make it possible to obtain nanoparticles with average sizes of 54.1 ± 5.0 nm, 99.1 ± 1.0 nm and 161.5 ± 4.4 nm, when the phase inversion temperature, high shear homogenization or the solvent injection techniques were respectively used. All optimized formulations showed a narrow size distribution and the zeta potential values were between -20 and -38 mV depending on the technique used. The three colloidal suspensions were considered physically stable at room temperature for at least three months as no significant changes in mean size, polydispersity index or zeta potential values were observed. The gel formulations exhibited viscosities of 32 800 ±100 mPa.s with pH values of 5,0 ± 0,5. In order to evaluate their potential as a new carrier system for skin delivery and as a follow-up to these promising initial results, morphological analysis of the nanosystems and evaluation of their encapsulation capacity are in progress, before in vitro skin permeation and retention studies are considered.

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IMPACT OF DIFFERENT PHOSPHOLIPID-BASED EMULSIFIERS ON PHYSICAL STABILITY OF TOPICAL MULTIPHASE SYSTEMS AND THEIR EFFECTS ON CELL VIABILITY

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Phospholipids are interesting candidates for a variety of applications, both in the pharmaceutical and cosmetic sector. As constituents of cellular membranes, they are known for their high biocompatibility and skin-friendliness [1]. These promising properties and their great emulsifying powers renders them suitable for preparation of various formulations [2]. For the present study, we developed aqueous dispersions and o/w nanoemulsions with 5% (w/w) phospholipids and conventional surfactants. The formulations were characterized and their stability was assessed over 8 weeks. In further research, we aim to investigate the effect of the prepared formulations in combination with UVA radiation on human skin cells. For preparation, the surfactant was dissolved and the oily phase was slowly added to the aqueous phase, followed by prehomogenization with a rotor/stator mixing device and treatment with a high-pressure homogenizer. The formulations were stored at either 8 °C or 21 °C to evaluate the influence of different storage conditions. Tested parameters included droplet size, PDI, zetapotential, pH and rheological properties. After preparation, the nanoemulsions exhibited satisfying homogeneity (PDI < 0.2). With one exception, zeta potential values were > ±30 mV, indicating good long-term stability. After 8 weeks, most phospholipid-based formulations showed a decrease of pH and increase of droplet size. In most cases, changes were more pronounced when stored at 21 °C. We are currently working on assessing the phototoxic potential of the prepared formulations in vitro. As recommended by OECD guidelines [3], we are employing the NRU phototoxicity assay. This assay compares the cytotoxicity of investigated substances when tested in presence vs. absence of exposure to simulated solar light. Primary skin cells will be treated with the respective formulation and exposed to UVA radiation. Cell viability will be measured and compared to a control plate that was prepared simultaneously, but not irradiated. To conclude, various dermal formulations were prepared and their stability under different storage conditions was assessed. In general, phospholipid-based formulations showed better stability when stored at 8 °C, although 2 formulations expressed good results when stored at 21 °C. In ongoing studies, we are investigating the phototoxic potential of the prepared formulations to evaluate the suitability of phospholipid-based emulsifiers for sunscreen development.

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INFLUENCE OF IONTOPHORESIS ON TRANSDERMAL DELIVERY OFKETOPROFEN LOADED DEFORMABLE LIPOSOMES INTO THE SYNOVIALFLUID: IN VITRO AND IN VIVO EVALUATION

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Objective of the study was to formulate negatively charged deformable liposomes (DL) using biosurfactants to enhance intraarticular delivery of ketoprofen (KP) under the influence of iontophoresis on transdermal application. KP deformable liposomes (KP-DL) were prepared using thin film hydration method using different lipids (phospholipon 90H, soya phoshphotidylcholine and Epikuron 200SH), with and without biosurfactants (Sodium cholate and sodium deoxycholate), characterized and intraarticular delivery of KP was evaluated. Using Sprague-Dawley rats, implantation of microdialysis probe and probe recovery was optimized, KP concentrations in the synovial fluid was measured using HPLC. Availability of KP was determined from synovial fluid concentration versus time plot by calculating dermatopharmacokinetic parameters (Phoenix WinNonlin® software). Vesicles displayed entrapment efficiency (>71 %); zeta potential < -25 mV; size was between 152.4 ± 12.42 nm to 220.4 ± 6.22 nm, KP-DL formulations were stable under iontophoresis. Conventional and deformable liposomes exhibited relatively higher iontophoretic flux values than passive flux. Maximum concentration (Cmax) in the synovial fluid achieved with KP-DL2 iontophoresis (0.24 ± 0.02µg/ mL) was 2-fold higher than DS- intravenous administration (0.0.11 ± 03 µg/mL respectively). It was observed to be relatively higher than DL-SC passive (0.146 µg/mL) at the end of 6h (tmax). AUC0- 8h was 0.329 ± 0.15 µg.h/mL (KP-DL2 passive) and 1.34 ± 0.12 µg.h/mL (KP-DL2 iontophoresis), clearly indicating 4-fold increase in drug availability in presence of iontophoresis (P < 0.001). Cathodal iontophoretic drug transport from the DLs was significantly higher, as demonstrated by lower passive flux in comparison to iontophoretic flux. Hence, data obtained reveals that iontophoresis could aid in transport of ketoprofen delivered via deformable liposomes into joints bypassing the dermal circulation and sub-dermal tissues and provide adequate concentrations in the synovial fluid to exert analgesic effect.

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LIPOSOMAL ENCAPSULATION AND RELEASETO PROTECT AND TREAT THE SKIN

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The skin is the first protective barrier against environmental aggressions. For an optimal drug permeation through it, the composition of the delivery systems should be controlled and optimized, been its lipid composition of crucial relevance. Liposomes for the transdermal drug delivery has been widely studied due to the high efficiency achieved together with the advantages of using this route of administration [1]. Knowing the hydrophilic-hydrophobic properties of liposomes, they can be used as vehicles and at the same time work to protect the skin from external aggressions. In precedent publications [2] our group demonstrated the capacity of nano-encapsulation of active ingredients in liposomes of an optimized lipid composition, obtaining better permeations through the skin than commercial formulations. This improvement was due to the creation of lipid layers on the stratum corneum capable of releasing the encapsulated active principle in a sustained manner over time [3]. In the present communication, we developed a specific liposome formulation with superior properties by comparing them with classic ones, such as ointments with free components. Liposomes with active principles (AP) include two natural extracts, Rosa eglanteria and Centella asiatica, which have epithelializing and healing activity [4, 5] as well as ZnO that also brings healing activity [6]. These new formulations are particularly indicated for treating wounds and scars that are permanently exposed, such as derived from lupus, scar regeneration or the treatment of recurrent wounds in patients who spend long periods in bed. The final formulations containing multilamellar liposomes demonstrate the capacity to provide a double boost release through the skin, with a fast delivery of the free AP followed by a delayed release of the AP from the liposomes. This double boost increases more than two times the amount of AP found in the tissue observed during the permeation assays showing lower Kp values than the free AP. Also, atomic force microscopy imaging show how the presence of liposomes smooths the skin surface creating a layer of lipids over it, providing protection and an occlusive effect into the wounds. All these data demonstrate that the liposomal formulations provide a higher delivery of PA through the skin compared with the free AP. Consequently, these formulations could speed up the healing process of these difficult-to-heal wounds compared to the traditional formulations.

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INFLUENCE OF IONTOPHORESIS ON TRANSDERMAL DELIVERY OFKETOPROFEN LOADED DEFORMABLE LIPOSOMES INTO THE SYNOVIALFLUID: IN VITRO AND IN VIVO EVALUATION

NANOSTRUCTURED LIPID CARRIERS AS A PROTECTIVE NANORESERVOIR OFHYPERFORIN IN ST. JOHN'S WORT EXTRACT: PRELIMINARY STUDIES

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One of the primary reasons for the ongoing research in wound care is the lack of a product with a complex therapeutic effect. Among phytochemicals possessing antioxidant, anti-inflammatory, and antibacterial properties, hyperforin (HP) in St. John's wort (SJW) stands out with its further ability to promote keratinocyte differentiation. Despite its promising characteristics, the therapeutic potential of this prenylated phloroglucinol is hindered by its sensitivity to light and oxygen [1]. Regarding HP's hydrophobic nature, its inclusion in nanostructured lipid carriers (NLCs) could preserve its stability and allow its topical application. In this study, NLCs were developed by emulsification, high-shear homogenization, and ultrasonication. By varying the solid (beeswax (BW) and glyceryl behenate (GB)) and liquid (almond oil (AO) and borage oil (BO)) lipids used, as well as the processing parameters (homogenization speed and ultrasonication time and temperature), twenty models were obtained [2]. The models that exhibited preferable properties were loaded with SJW extract, rich in HP, by initially incorporating it in the lipid phase [3]. The blank and extract-loaded NLC systems were relatively homogenous (polydispersity index (PI) lower than 0.3), comprising nano-sized particles (with mean diameters smaller than 200 nm) with high zeta potential (ZP) values (>|30| mV). ATR-FTIR studies confirmed the presence of HP-rich SJW extract in the HP-NLCs and the suitability of the selected extract concentration. The successful encapsulation was also proven by the HPLC-assessed entrapment efficiency (EE) values higher than 70%. The less-ordered inner structure of nanoparticles (compared to the solid lipid used) was demonstrated by their XRD pattern. The carriers' inner morphology was also investigated by TEM, and colloidal particles with imperfect matrices were observed [3]. The model showing greater entrapment ability and desirable PI and ZP values after a month of storage at 4°C was chosen as a carrier of HP-rich SJW extract. Based on the obtained results, the elaborated NLC may be considered a promising colloidal system for preserving the susceptible phytochemical in SJW extract. This work was funded by the Fund "Nauka" at the Medical University of Varna, Bulgaria, through Project No. 18027.

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TRANSFERSOMES FOR CUTANEOUS AND LYMPHATIC TARGETING OF ROSE BENGAL TO TREAT MELANOMA

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Melanoma accounts for 1.7% of global cancer diagnoses, and survival for stage IV disease is 29.8%.1 Rose Bengal (RB) is a photosensitive water-soluble dye that emerged as intralesional therapy for advanced cutaneous melanoma. However, RB photodegrades and poorly crosses biological membranes; also, adverse effects of the intralesional route were reported (injection site pain, erythema, swelling, photosensitivity).2 Thus, RB-loaded Transfersomes (RBTF) were designed for RB delivery to melanoma cells via cutaneous administration. RBTF were prepared and characterised (size, ζ-potential, RB loading, morphology, in-vitro RB release, ex-vivo epidermis permeation); an antiproliferative assay on melanoma cells was carried out.3 Then, RBTF were included in trilayer polymeric dissolving microneedles (RBTF-TDMNs) to control RBTF intradermal delivery. RBTFTDMNs mechanical properties were evaluated. An ex vivo dermatokinetic study determined RBTF-TDMNs intradermal delivery efficiency.4 Finally, an in vivo study was performed on healthy Sprague–Dawley rats to assess the pharmacokinetics of RBTF and the lymphatic targeting via intradermal (i.d.) injection by hollow microneedles (RBTF-HMNs) (24 hours) (600 µm length, Nanosoft®); as a comparison, RBTF were administered via intravenous (i.v.) injection (2 h). RB solution was also tested by the same routes. RBTF were about 100 nm (0.2 PDI) with a -45 mV ζ-potential; RB strongly interacted with lipids originating unilamellar and deformable RBTF and determining no release of RB at 37°C for 48 h. RBTF doubled RB's amount permeating the epidermis and reduced melanoma proliferation compared to RB, increasing cancer cell selectivity. RBTF-TDMNs were strong enough to pierce the skin, where they rapidly dissolved to release RBTF without altering their structure. RBTF-TDMNS increased the RB amount deposited in the skin compared to the RBTF dispersion. After i.d., the AUC of RBTF was higher than the AUC of RB solution ($p<0.01$) and lymph node uptake was highest for RBTF (2 h). After i.v., no differences in the pharmacokinetics of RBTF and RB solution were observed; from the blood, RBTF and RB solution couldn't reach the lymph nodes. To conclude, RBTF were a valid tool for RB delivery to melanoma cells via cutaneous administration. If RBTF-TDMNs could assist the management of early-stage melanoma, RBTF-HMNs could prevent metastatisation, allowing RB lymphatic targeting.

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BI-GEL: AN INNOVATIVE TOPICAL DOSAGE FORM. A CASE STUDY WITH LAVANDULA ANGUSTIFOLIA ESSENTIAL OIL

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The efficacy, tolerance and application properties of dermatological products are clearly related to the type of base used. The interactions between the base, the skin and the drug influence the different effects of the preparation and the release of the drug. There are a variety of vehicles that allow a given therapy to be tailored to the condition of the skin. As such, bi-gel, widely used in the cosmetics and food fields, is an emerging and innovative topical pharmaceutical form which has many advantages[1]. Bi-gel is an intimate mixture of an aqueous gel and an oily gel. Due to its dual nature, this system is suitable for both lipophilic and hydrophilic drugs, with good ability to transport drugs through the skin[2]. The absence of any surfactant enables to develop high tolerance formulations with unique characteristics: refreshing sensation, natural moisturizing properties and excellent ease of application. Indeed Emulfree® Duo, an oil stabilizer, is composed of a synergistic combination of emollients and ethylcellulose, which stabilize the system. Depending on the concentration of Emulfree® Duo used, a palette of textures, from sprayable lotion to rich cream, can be designed. The entire process can be carried out at room temperature: this energy-efficient process is ideal for heat-sensitive drugs and to minimize manufacturing costs and risks. This study aims to propose an natural alternative for topical formulation with Lavandula angustifolia for the antiinflammatory treatment. Various oily vehicles (Labrafac™ Lipophile WL1349, sweet almond oil, mineral oil), gelling agents (Carbopol Ultrez 10, Carbopol EDT 2020, Sepineo P600, Pemulen TR1 NF, Xanthan gum) and thickeners (Cetostearyl alcohol, hydrogenated castor oil, Geleol™ mono and diglycerides NF, Compritol® 888 pellets) were screened to determine the optimized composition of the bi-gel, regarding its stability, macroscopic/ microscopical aspect, and its sensorial profile (based on placebo formulation). Based on these criteria and depending on the surface to treat, different formulations are recommended: sprayable lotion, creamy or rich cream-like textures.

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Key word = bi-gel, Emulfree® Duo, surfactant-free, oil stabilizer

BORAGE OIL-BASED BIGELS FOR TOPICAL DELIVERY OF NANOENCAPSULATED ST. JOHN'S WORT EXTRACT: TEXTURAL AND RHEOLOGICAL CHARACTERIZATION

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Hyperforin (HP) in Hypericum perforatum L. is a light- and oxygen-sensitive phytochemical well-known for its woundhealing properties. For that reason, in our preliminary studies, a nanostructured lipid carrier (NLC) system for preserving HP in St. John's wort (SJW) extract was elaborated [1]. In order to allow its topical application, the nanodispersion should be incorporated into a semisolid formulation. As a vehicle, bigels were chosen; these hybrid structures contain hydro- and oleogels and combine their advantages while overcoming each's limitations [2]. Eight different bigels (blank and HP-NLC-containing) of different hydro- and organogel proportions (from 90:10 to 60:40 in favor of the hydrophilic phase) were obtained. Poloxamer 407 (20%, w/w) was dissolved in purified water (or purified water mixed with HP-NLC to provide a 0.5 w/w% final extract concentration) at 4°C for 24 h. After obtaining a semisolid structure by equilibrating the solution to room temperature, the hot oleogel (containing 15w/w% sorbitan monostearate dissolved in heated to 60 ± 2°C borage oil) was added to it portion-wise and stirred at 1000 rpm for 10 min. To select the preferable one, the formulations' physicochemical, mechanical, and rheological properties were investigated [3]. All bigels "passed" the tube inversion test, but the models containing 40% lipophilic phase were very greasy and were excluded from the study. The remaining formulations possessed skin-tolerable pH values and were proven stable under a centrifugation test. Through rheological studies, the expected pseudoplastic flow was confirmed for the semisolids. The relationship between the increasing oleogel fraction and the spreadability, firmness, cohesiveness, and adhesiveness of the bigels was demonstrated by textural analysis [3]. Our investigations concluded that superior consistency and structural integrity were achieved in the formulations containing hydrogel and oleogel in an 80:20 ratio; therefore, the latter was chosen as a vehicle for NLC-encapsulated HP-rich SJW extract. The elaboration of a suitable semisolid platform would ensure sufficient skin contact time and unfold its woundhealing potential. This work was funded by the Fund "Nauka" at the Medical University of Varna, Bulgaria, through Project No. 18027.

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DEVELOPMENT & CHARACTERIZATION OF CALCITRIOL LOADED IN-SITU GEL FORENHANCING ORTHODONTIC TOOTH MOVEMENT

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Orthodontics is derived from two Greek words “orthos” means correct and “odont” means tooth. Therefore, it is a branch of dentistry which deals with the irregularities of teeth e.g., straightening of crooked tooth or reduction of gap present between the teeth. In orthodontic treatment there is an application of force (braces) on the teeth to align them properly. But the main drawback of this treatment is that it is a very lengthy process and usually takes around 2 years or more to get complete. Some side effects related to longer orthodontic therapy are demineralization, root resorption etc. So, there is an urgent need to develop a novel formulation that will enhance the tooth movement during the orthodontic treatment and will ultimately decrease the treatment time. Therefore, the purpose of this study was to formulate and characterize calcitriol loaded in-situ gel for enhancing orthodontic tooth movement. Calcitriol, Methanol, Kolliphor P 407etc. these are some of the materials used in the preparation of in-situ gel by using cold process method. During trial 11 formulations were prepared. Among all the formulations, formulation F11 was selected for further evaluation on the basis of its gelation time. Formulation F11 converts into gel within 4 seconds at body temperature. The prepared formulation F11 was then evaluated for various parameters like clarity, pH, drug content, FT-IR, gel strength, syringeability, in-vitro drug release and ex-vivo drug permeation studies. In the UPLC analysis, the representative sample (10µg/ml) of Calcitriol showed major peak at 265 nm. Drug content of the prepared formulation was found to be 98.3% whereas the pH of the formulation was 7.00 which resembles the pH of mouth. The prepared formulation was also evaluated for in-vitro drug release and ex-vivo permeation study at predetermined rate (15 sec., 30 sec, 45 sec., 60 sec., 90 sec., 120 sec.,) and was found that the formulation release 95% of drug at 60 sec. during in-vitro drug release study and 65% of drug at 60 sec. during ex-vivo permeation study. From this study it was concluded that owing to the gelation capacity of the polymer the prepared formulation was planned to deliver at the local site (gums) in the form of liquid drops which were then converted into gel within seconds due to temperature changes. Based on the preliminary results it can be stated that the developed formulation holds good potential to be used in orthodontic treatment with reduced side effects.

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EFFECT OF POLOXAMER 407 / BORAGO OIL BIGEL CONTAINING METHANOL EXTRACT OF ST. JOHN'S WORT LOADED NANOSTRUCTURED LIPID CARRIERS IN SKIN WOUND APPLICATION ON BLOOD LIVER AND KIDNEY DAMAGE

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The aim of the study was to investigate the toxic effects of the skin wound application of a Poloxamer 407 / Borago oil bigel (B) containing methanol extract of St. John's wort (SJW) loaded nanostructured lipid carriers (NLC-SJW) compared to a bigel with the same extract and a commercial product (CP). A control group was included in the study to serve as a reference for any changes in treatment groups (wound healing: G0; CP wound treatment: G1; B/SJW wound treatment: G2 and B/NLC-SJW: G3). G1, G2, and G3 applications were performed for 2-, 7-, 14- and 21-days periods (D2, D7, D14, and D21). To check for possible toxic effects of G2 and G3 treatments or their possible protective potential in the condition of skin injury, GGTP, AsAT, AlAT, and LDH enzyme levels were measured as indicators for liver damage. GGTP levels were elevated by 185% ($p<0.001$) and 120% ($p<0.05$) in G2 and by 142% ($p<0.01$) and 175% ($p<0.01$) in G3 as compared with the control group in D2 and D7, respectively. GGTP levels normalized at D14 and D21, where their levels did not differ from the control group. What is more, GGTP levels in G3 treatment at D21 were 64% ($p<0.05$) lower than in G0 animals. 2D application of SJW in the two formulations (G2 and G3) contributed to normalized AlAT levels that were 27% ($p<0.001$) and 25% ($p<0.05$) lower than in the skin injured rats (G0) that were with AlAT levels higher than the control group (88.02±8.37 vs. 59.85±7.41 U/L). Similarly, at D7 LDH levels were normalized in G2 and G3 groups, where SJW extract application contributed to 58% ($p<0.05$) and 67% ($p<0.05$) LDH decrease, compared to G0, where LDH levels were significantly increased by skin damage (389.42±164.14 vs. 128.36±68.45 U/L). AsAT levels were lower in D21 in both G2 and G3 formulations than in control and G0 animals, but the difference was significant in the G2 group only (by 24%, $p<0.05$ vs. control and by 19%, $p<0.05$ vs. G0). Total protein and renal function indices (urea, creatinine, and uric acid) remained unchanged in all groups, except for the slight but significant decrease (6%, $p<0.05$) in urea levels in the G2 group vs. control.
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FORMULATION AND IN VITRO PERMEATION EVALUATION OF NSAID DRUG MICROEMULGEL

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NSAID anti-inflammatory agents are widely used to decrease inflammatory, pain and fever. Their topical forms are very interesting to treat rheumatoid arthritis. Unfortunately, majority of them present low cutaneous permeability (1,2). The aim of this work is to encapsulate different NSAID drugs in microemulgel form and evaluate the in vitro skin permeation. Three NSAID were selected and used as models. Microemulsions were prepared by titration method and gelling was obtained by addition of carbopol 940 gel (1 to 2%). Size, Zeta potential, transmittance and refractive index were measured. The in vitro permeation test was conducted with Franz diffusion cell technique. Microemulgel releases profiles presented promising results to improve cutaneous permeation and can be used efficiently as an alternative to oral and conventional NSAID forms.

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Keywords: arthritis, cutaneous, Franz cell, microemulsion, permeation.

STUDY OF THE BIOMECHANICAL PROPERTIES OF A HYDROGEL LOADED WITH PRANOPROFEN LIPID NANOPARTICLES

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Pranoprofen (PF), also known as 2-(5H-chromeno[2,3-b] pyridin-7-yl) propanoic acid, is a strong NSAID that is used to treat inflammation, fever, and pain [1]. Nanostructured lipid carriers (NLC), a subset of drug-delivery nanosystems, have drawn attention as dermatological formulations for drug delivery because of their small size, biocompatibility, capacity to incorporate lipophilic and hydrophilic drugs, drug protection, and controlled release properties. These colloidal nanocarrier systems provide an imperfect crystalline matrix that enables the solubilization and incorporation of the drug into the lipid. They are made up of a mixture of liquid lipid (oil) and solid lipid [2]. Dermatological therapeutic products aim to increase drug retention in the skin by modulating its permeability, which can be achieved by using penetration enhancers to reduce barrier resistance and improve transdermal drug delivery. The main goal of this work was to evaluate the biomechanical properties on the flexor side of the left forearm of a selected hydrogel of Poloxamer-based loaded with pranoprofen (PF-NPP407) and additionally to study its extensibility property. The high-pressure homogenization technique was used to produce the NLC. Milli-Q water was mixed with Poloxamer 407 and stirred magnetically. The hydrogel was chilled for 24 hours and then added NLC. The formulation's final concentration was 10.7 mg PF/g gel, and the particle size was assessed. Transdermal water loss (TEWL) and stratum corneum hydration (SCH) have evolved as biomechanical metrics. After applying PF-NPP407 hydrogel to the skin, a statistically significant decrease in TEWL values was observed, which explained an occlusive action without affecting skin integrity. The SCH nevertheless experienced a small boost. These results showed that the formulations marginally enhanced the hydration compared to the skin's typical behavior, which is consistent with the fact that skin capacitance is directly related to skin hydration. Additionally, no visible skin irritation was seen when the PF-NP-P407 hydrogel was applied to the skin of the volunteers, indicating that the hydrogel was well tolerated. Moreover, extensibility analysis fitted the mathematical modelling one-phase exponential association kinetic profile for the hydrogel.

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THREE-DIMENSIONAL SCAFFOLDS OF CHITOSAN WITH ANTIBACTERIAL PROPERTIES FOR SKIN TISSUE ENGINEERING APPLICATIONS.

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Three-dimensional (3D) printing has seen a rapid technological development over the last two decades [1]. 3D printed patches are fabricated for skin tissue engineering applications, promising solutions for medical treatments, particularly for healing of chronic wounds [2]. 3D printing technology fabricate scaffolds with flexible matrices with high precision, possessing well defined architecture and physical orientation [3]. A wide range of biocompatible synthetic and natural polymeric hydrogels have been used for the fabrication of 3D printed dressings. In this work, thermosensitive hydrogels based on chitosan (CS). CS is as a naturally derived polymer that plays a leading role in the development of new skin tissue engineering products [4]. CS is a cationic polysaccharide with bactericidal properties, renewable, nontoxic, biodegradable and hydrophilic with high reactivity, promotes coagulation, flocculation and biosorption. The antibacterial properties of CS are due to direct electrostatic interactions between negatively charged bacterial and the positively charged CS. Researchers and pharmaceutical companies are focusing on the antibacterial properties of CS by formulating it into several skin engineering products. Hydrogels based on CS were synthesized and their viscosity and printability were studied. The 3D printing conditions such as temperature, pressure, and needle size were optimized, and 3D printed scaffolds were fabricated. Subsequently, the swelling capacity, hydrolysis rate the cytotoxicity and antibacterial activity were researched.

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TOPICAL DELIVERY OF METRONIDAZOLE USING A GREEN-CROSSLINKED GELATIN-BASED HYDROGEL SHEET-MASK FOR THE TREATMENT OF PPERELATED SKIN-LESIONS

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Personal protective equipment (PPE) exerts continuous pressure, tension, and friction forces on the skin, as well as an increase of temperature and humidity, responsible for the appearance of skin lesions1. Flare-up rosacea in healthcare professionals (HCP) has been reported as one of the most common PPE-related skin lesions, alongside with "maskne" and dermatitis2. A two-in-one treatment to avoid this skin lesion and rosacea would be a product that could function as a protective skin barrier as well as deliver system of metronidazole. In this work, gelatin was crosslinked using a green and non-toxic ingredient, acid tannic, and a gelatin-acid tannic-based hydrogel sheet-mask was developed and characterized to function as a metronidazole delivery system and a protective skin barrier dressing. Gelation temperature, compression, adhesive and tribology studies were performed to evaluate the adaptability of the hydrogel sheet-mask under conditions provided by the mask use using a Kinexus Lab+ Rheometer. A target force of 0.7N and 4N were used to simulate the pressure exerted by surgical and FFP2 mask, respectively. To comprehend the lubricant properties, a constant force was exerted using tribometer at 25°C and 32°C. To evaluate the in vitro release of metronidazole using Franz diffusion cells, an occlusive system using part of a surgical mask was performed. This strategy was developed to simulate the moist environment provided by the prolonged and continuous use of PPE, and how it impacted the drug release. A gelation temperature of 46.92 ± 2.69 °C indicates that gelatin was effectively crosslinked. Compression test demonstrated complete elastic recovery with adhesive properties in both tested forces. Tribology has demonstrated that the product maintained its structure when submitted to conditions simulating the mask use. In vitro results showed an initial high burst release, reaching about 30% of metronidazole released after 1 hour in both cases. A release of 52.63% was observed in the samples with the mask placed on top of the sheet-mask after 4 hours, while in case samples without the mask the release was of 62.63%. This suggests a diffusion of metronidazole occurred on the materials composed by the mask. In conclusion, the resistant physical properties and the drug release capability of this hydrogel sheet-mask is a good indication that this polymeric film-forming system can prevent skin lesions and avoid the appearance of rosacea during mask usage.

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«EX VIVO» TRANSDERMAL STUDY ON HUMAN SKIN OF A BARICTINIB MICROEMULSION

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Baricitinib is a Janus kinase inhibitor that has been approved for the treatment of rheumatoid arthritis and specific cases of atopic dermatitis. It is a slightly water-soluble drug that is administered orally [1]. The dermal route is a non-invasive alternative for drug administration. However, the characteristics and particularities of the tissues and the existing barriers limit the bioavailability of the drug, hence, strategies to increase drug solubility and overcome the skin barriers are often required in topical delivery. This can be achieved for example by using physical or chemical enhancers and formulating the drug in microemulsions. Microemulsions are described as isotropic, transparent, and thermodynamically stable. Their stability, ease of formation, and small droplet size of 20-200 nm make them an ideal vehicle for drug delivery [2]. The objectives of the study were to develop a baricitinib microemulsion for topical administration and to evaluate the penetration of the drug through human skin. Franz diffusion cells were used for the permeation study of baricitinib formulated in the microemulsion. The test was conducted at 32°C for 30 h and within this period, sample aliquots were taken at different time intervals and analyzed by HPLC to determine the concentration of the drug permeated. The following permeability parameters were determined: flow (J), lag-time time (TL), amount of drug retained in the skin at 30 h (AR30h), permeability coefficient (Kp), and the concentration that would be reached in the steady state (Css). The flux was calculated considering the linear part of the permeation profile, which was 2.19 ± 0.57 µg/h/cm2; the lag-time was estimated as the intercept in X-axis, which was 11.85 h; the amount of drug retained in the skin was 631.16 ± 113.61 µg/cm2, the coefficient of permeability was 4.4 ± 0.4 x 10-4 cm/h, and the Css was estimated considering the human plasma clearance of baricitinib of 2.32 ± 0.39 ng/mL and a theoretical transdermal area of applied formulation of 1 cm2. The concentration would be assumed to be below the systemic therapeutic concentrations reported by the oral route [3].

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Keywords: Baricitinib, Microemulsion, Permeation.

COSMETIC PICKERING EMULSIONS STABILIZED BY NATURAL SOURCE OF PROTEIN-BASED PARTICLES

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The current challenges and emerging research trends address using natural origin, renewable, sustainable and environmental friendly emulsifiers systems (1). As early as the beginning of twentieth century, both Ramsden and Pickering found solid particles to be interfacially active and able to stabilized emulsions (2; 3). In response to the growing consumer interest in naturality, there is a renewed enthusiasm for studying the functionality of different natural-based particles. Proteins have long been recognized as excellent for Pickering emulsion thanks to their good interfacial and emulsification activities. The low level of solubility of natural origin proteins in aqueous media and oils is now likely to be considered as a valued functional attribute by researchers working on Pickering systems (4). They also have the ability to function as stabilizers and thickening agents in the form colloidal particle (5) and they have fast interfacial adsorption kinetics (6). Liquid emulsion droplets stabilized by colloidal particle via the Pickering stabilization mechanism are highly resilient towards coalescence and Ostwald ripening as compared with conventional dispersions stabilized by surfactants or polymers (7). This feature allows for the protective storage of ingredients that are sensitive to environmental conditions such as light, oxygen and heat (8). The “surfactant-free” character makes the Pickering emulsion attractive to life sciences where surfactants often cause either irritancy. Additionally, Pickering emulsions behave as penetration enhancers. The skin permeation of active molecules loaded inside the droplets of a Pickering emulsion was faster than for a conventional emulsion or a homogeneous solution. Although the mechanism of accelerated transport is not clearly established there are definite differences with respect to surfactant-based emulsions (9). Colloidal particles that originate from natural biomolecules are being developed as Pickering particle and applied in cosmetics fields. Excellent interfacial activity, biocompatibility, biodegradability and amenability for surface modification made protein bases particles stand out as candidate Pickering emulsions (8).

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DEVELOPMENT OF A CRISABOROLE NANOEMULSION FOR THE TREATMENT OF ATOPIC DERMATITIS.

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Atopic dermatitis (AD) is the most common inflammatory skin condition among the adult and child population that leads to a decrease in the quality of life of patients. Currently, there is no curative treatment for the pathology; however, new therapeutic options are being sought for a safe and effective treatment. Crisaborole is a novel non-steroidal anti-inflammatory drug which acts by selectively inhibiting the enzyme phosphodiesterase 4, to control cAMP levels. The aim of this work was to develop a crisaborole nanoemulsion (NE) in order to improve the penetration, absorption and bioavailability of the active ingredient. The solubility of crisaborole was evaluated in oils, surfactants and co-surfactants. Four pseudo-ternary diagrams were constructed in order to establish the composition of crisaborole NE (CR-NE) which was characterized physically, chemically and biopharmaceutically. Physicochemical characterization included pH, rheological behavior, droplet size, polydispersity index and morphological evaluation. Efficacy was tested using an in vivo mouse ear model. The inflammatory process was induced by the topical application of xylene on the right ear. The composition formula of CR-NE consisted of Lauriglicol 90, tween 80, Transcutol P and water. This formulation presented a pH value of 5.02 ± 0.003, a mean droplet size around 109,4±3,97 nm with a PI value of 0,27±0,014, spherical shape, viscosity of 48,76±0,01 mPa·s and Newtonian behavior. The release profile followed a hyperbolic kinetic. Finally, the efficacy studies revealed that topical administration of xylene triggered vasodilation and erythema, whereas the group which was treated with CR-NE afterwards to induce inflammation showed a significant decrease in the inflammation which was evident through deep histological analysis. Consequently, these results suggest that CR-NE can be applicated in topical form without causing irritation or damage to the skin and be used as an alternative treatment for inflammatory skin diseases such as atopic dermatitis.

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DEVELOPMENT OF A MICRO-EMULSION CONTAINING CANNABIDIOL FOR TOPICAL USE: A PRE-FORMULATION STUDY

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Cannabidiol (CBD) is a safe and non-psychotropic phytocannabinoid with a wide range of potential therapeutic uses. Due to its lipophilicity, it is normally available dissolved in oily phases. The main aim of this work was to develop and characterize a new formulation of a microemulsion obtained from a CBD oil as hydrophobic phase, Labrasol/Plurol Oleique (1:1) as surfactant and cosurfactant (S/CoS) respectively and water. A pseudo-ternary phase diagram was elaborated, selecting an optimal proportion of 62% (S/CoS), 27% CBD oil and 11% water. The defined system was characterized in terms of conductivity, droplet size by laser scattering, compatibility of components by differential scanning calorimetry and rheological properties using a rotational rheometer. The designed microemulsion showed good compatibility and stability showing a slight pseudo-plastic behavior. The release properties of CBD from the microemulsion and the CBD oil was studied by in vitro diffusion experiments using flow-through diffusion cells. It was evidenced that the inclusion of the original oil in a microemulsion did not provoke a significant modification of the release of CBD, incorporating the possibility of including hydrophilic compounds in the formulation, establishing an interesting strategy for the development of future formulations.

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EX-VIVO SKIN RETENTION AND PERMEATION OF CRISABOROLE FROM INNOVATIVE TOPICAL FORMULATIONS

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Crisaborole is a non-steroidal phosphodiesterase 4 (PDE4) inhibitor, approved in 2016 by the FDA for the treatment of atopic dermatitis (AD) in adults and children greater than 2 years of age (1). Moreover, its off-label use has highlighted its effectiveness also in the treatment of other inflammatory skin disorders such as psoriasis, seborrheic dermatitis, vitiligo, and inflammatory linear verrucous epidermal nevus (2). Although its mechanism of action is still not known, several clinical trials demonstrated its efficacy and safety and recently it has been approved for use in children as young as 3 months of age for the treatment of AD. The aim of this work was the ex-vivo evaluation of crisaborole skin retention and permeation from innovative topical formulations. In particular, we focus on microemulsions (MEs). Skin retention of crisaborole from the prepared formulations, applied in finite dose conditions (10 µl/cm2) for 4 or 24 h, was evaluated using porcine ear skin in Franz vertical diffusion cells. The commercial 2% crisaborole ointment Eucrisa (Pfizer) was used as reference. Two MEs were prepared, one o/w (ME Tween) and one w/o (ME Peceol), to assess the effect of ME type on crisaborole skin retention. Both MEs contain relevant amounts of Transcutol as co-surfactant, because it guarantees high drug solubility, and were saturated with crisaborole (final concentration 13 and 18 mg/ml respectively for ME Tween and ME Peceol). After 4 h of contact, crisaborole accumulated both in epidermis and dermis from all the formulations tested, but did not cross the skin in significant amount, with the exception of the commercial formulation. In the epidermis, Eucrisa produced greater drug retention compared to MEs which in turn produced performances similar to each other. In the dermis, no difference between formulations can be observed. After 24 h the three formulations performed in a very similar way with the only exception of a significantly lower retention ($p<0.05$) in the epidermis in the case of ME Tween and a significantly higher permeation ($p<0.05$) in the case of ME Peceol. When the ratio amount retained/permeated was calculated, the ranking of formulations was the following: Eucrisa>ME Tween>ME Peceol. In general, the two MEs gave comparable performance; the ME Tween (o/w) was slightly better but had a slightly higher crisaborole concentration, suggesting that the drug might be associated with the co-surfactant at the interface.

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EYE IRRITATION POTENTIAL OF RED RASPBERRY SEED OIL AFTER NANOEMULSIFICATION: ASSESSMENT WITH THE HET-CAM TEST

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Nanoemulsions, especially those prepared by low-energy processes, have recently been proposed as promising carriers for natural products such as plant oils and extracts. The main reasons for their great potential in cosmetics are: interesting visual appearance and targeted/controlled release of active ingredients; good application properties and light skin feel; cost efficiency due to high water content and energy-saving manufacturing methods (1, 2). However, these novel carriers need to be thoroughly assessed, starting with their skin and eye irritation potential. Therefore, the aim of this study was to evaluate the eye irritation potential of pure red raspberry seed oil (INCI: Rubus idaeus seed oil) – RO, as a natural oil rich in polyunsaturated fatty acids, carotenoids, and tocopherols, suitable for various cosmetic formulations, and RO incorporated in nanoemulsion formulations prepared with different surfactants (polysorbate 80–P80 or polyglycerol ester –PG). The method used was DB-ALM Protocol n° 96: Hen's Egg Test on the Chorioallantoic Membrane (HET-CAM) Eye Irritation Assay, which was performed after the corresponding eggs were prepared in the egg incubator (conditions: temperature - 37.5±0.5oC, relative humidity: 55%±7%, rotation frequency: every 3-6 hours) (3). The tested samples, including the pure RO and P80/PG nanoemulsions (empty or loaded with RO), showed no signs of skin irritation as previously described (2). However, the results of the HET-CAM test showed that pure RO did not cause eye irritation, whereas there were significant differences between the nanoemulsions prepared with different surfactants. For example, the empty P80 nanoemulsion was classified as non-irritant, the P80 nanoemulsion loaded with RO as mildly irritant, while all PG nanoemulsions (empty or loaded with RO) showed some signs of irritation (moderately irritant). Although droplet sizes below 100 nm (as in our PG -nanoemulsions) are desirable, such small droplets can apparently increase the eye irritation potential of formulations, or this observation could possibly be due to the surfactant type per se. The results obtained clearly show that nanoemulsion carriers and/or surfactant type have a significant impact on the eye irritation potential of cosmetic actives.

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FORMULATION OF A MICROEMULSION CONTAINING CANNABIDIOL AND AN EXTRACT FROM S. EBULUS FOR POTENTIAL ANTI-INFLAMMATORY USE.

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The development of microemulsions is considered to be one of the most promising strategies for the concomitant formulation of highly lipophilic and hydrophilic compounds. The main objective of our study was to develop and characterize a new microemulsion system containing Cannabidiol (CBD), a lipophilic phytocannabinoid, combined with an aqueous extract of Sambucus ebulus L. for their potential synergistic antiinflammatory effect. This extract was firstly characterized, by HPLC, showing a high amount of polyphenolic compounds among others, selecting caffeic acid (CAF) as a reference fluorescent molecule to study the stability of the aqueous extract, once included in the formulation. The microemulsion contained a commercially available CBD oil (20%), as hydrophobic phase, Labrasol/Plurol Oleique (1:1) as surfactant and cosurfactant (S/CoS) respectively and the previously obtained and characterized extract as water phase. The microemulsion containing CBD and the vegetable extract was characterized in comparison to a previously defined microemulsion with purified water as aqueous phase, in terms of conductivity, droplet size and polydispersity analyses, rheological properties (rotational rheometry) and in vitro release properties of CBD form both formulations and CAF for the microemulsion containing the aqueous extract. It was observed that the inclusion of the extract did not interfere the release properties of CBD. The release constants for CBD and CAF were also determined. Slight differences of the rheological properties were observed. The creation of the bi-continuous system did not significantly affect the release of the CBD or the caffeic acid. This strategy appears as a promising galenical alternative due to its inherent advantages as a drug carrier for both substances.

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FORMULATION OF INNOVATIVE O/W EMULSIONS CONTAINING CURCUMIN DERIVATIVES WITH ENHANCED ANTIOXIDANT CAPACITY FOR SKIN APPLICATION

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Human skin's exposure to solar ultraviolet radiation (UVR) leads to a dramatic increase in the production of reactive oxygen species (ROS), resulting to deleterious skin diseases, such as aging, scaling, dryness, and ultimately, skin cancer, the most severe consequence of photodamage [1][2]. However, UVR and other free-radical generators can overwhelm the system, rendering the natural antioxidant compounds inadequate to protect the skin from the oxidative damage. Thus, cosmetic science has been receiving increasing attention towards the development of products with effective antioxidant agents. Topically applied antioxidants constitute an important group of pharmacologically active agents capable of inhibiting the oxidation of other molecules, thus protecting the skin cells against the damaging effects of ROS [3]. Lately, curcumin has arisen as an ideal candidate among other natural-derived components, due to its numerous phenolic groups leading to beneficial effects in several human disorders and its low toxicity. Curcumin (Cur) is a natural occurring lipophilic polyphenol located in the rhizomes of turmeric, also known as Curcuma longa, which has received recognition as a bioactive compound with great antioxidant properties. In the current work, a series of cosmetic formulations were prepared containing different Curcumin (Cur) derivatives in varying concentrations. Specifically, Cur powder at 0.5 and 2 % w/v ratios, Cur extract in water at 1% w/v ratio and 1% w/v ratio Cur complexed with -cyclodextrin were incorporated into Oil in Water (O/W) emulsions. Viscosity and pH measurements were performed to evaluate their stability during storage over time. Moreover, the effect of the active cosmetic substances on the antimicrobial and antioxidant properties of the prepared emulsions was investigated. It was observed that emulsions containing Cur extract and Cur ζ-cyclodextrin complex presented great viscosity and pH stability for up to 90 days of storage contrary to the emulsions containing Cur powder which showed unstable behavior due to the formation of agglomerates. The emulsions with Cur in all forms exhibited high antioxidant activity, whereas the emulsion containing Cur ζ-cyclodextrin complex presented the highest value. Despite their improved stability and antioxidant activity, the emulsions containing Cur extract and Cur-ζ-cyclodextrin exhibited a low percentage of antimicrobial activity against E. coli and Staphylococcus bacteria.

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FORMULATION, CHARACTERIZATION AND EVALUATION OF INNOVATIVE O/W EMULSIONS CONTAINING CURCUMIN DERIVATIVES WITH ENHANCED ANTIOXIDANT PROPERTIES

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Human skin's exposure to solar ultraviolet radiation leads to a dramatic increase in the production of reactive oxygen species (ROS), thus shifting the natural balance towards.[1]Several natural topical antioxidants have been already investigated, such as vitamin C [2], tea catechins [3], cinnamon leaf oil, table grapes [4], hippophaerhamnoides [5] and others. However, most of them are very unstable since they are easily oxidized and consequently lose their activity before reaching the target. Lately, curcumin has arisen as an ideal candidate among other natural-derived components, due to its numerous phenolic groups leading to beneficial effects in several human disorders and its low toxicity [6]. a pro-oxidative state and resulting in oxidative stress.
In the present study, a series of semisolid Oil inWater (O/W) emulsions containing different Curcumin (Cur) derivatives (Cur powder, Cur extract and Cur complexed with ζ-cyclodextrin) in varying concentrations, were prepared. Among them, Cur complexed with ζ-cyclodextrin was further characterized using Dynamic Light Scattering (DLS), microscopy, and its stability was studied in term of pH stability and viscosity measurements. Moreover, the effect of the active cosmetic substances on the Sun Protection Factor (SPF), and antioxidant properties of the prepared emulsions was investigated. It was observed that emulsions containing Cur ζ-cyclodextrin complex presented great viscosity and pH stability for up to 90 days of storage. All samples presented SPF values between 2.6 and 3.2. The emulsions forms exhibited high antioxidant activity, and among the prepared emulsions, the emulsion containing Cur ζ-cyclodextrin complex presented the highest value owning to the existence of bioactive polyphenols in the Cur structure. Overall, b-Cur emulsions exhibited high viscosity and pH stability, as well as an improved antioxidant activity.

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INNOVATIVE SKIN PRODUCT EMULSIONS WITH ENHANCED ANTIOXIDANT, AND UV PROTECTION PROPERTIES CONTAINING NANOPARTICLES OF CHITOSAN WITH ENCAPSULATED TANNIN

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Human skin's exposure to solar ultraviolet radiation (UVR) leads to a dramatic increase in the production of reactive oxygen species (ROS), thus shifting the natural balance towards a pro-oxidative state and resulting in oxidative stress [1]. In turn, oxidative stress induces undesirable and deleterious skin diseases, such as aging, scaling, dryness, mottled pigment, and, ultimately, skin cancer, the most severe consequence of photodamage [2]. So, adding UV protection and antioxidant agents in cosmetic emulsions could assist in the preservation of good skin health and the prevention of oxidative stress. Tannins are usually defined as polyphenolic compounds and present high antioxidant, anti-inflammatory, and UV protection activity. However, the skin forms a barrier to the external environment and is impermeable to the active agents so, there is a requirement for efficient delivery systems. Moreover, cosmetic emulsions including sunscreen agents can undergo a number of different instabilities such as gravitational separation, creaming, flocculation, coalescence and phase inversion. Nanotechnology can be used to modify active agents' permeation and improve the stability of emulsions. In the present work, chitosan (CS) was chosen for nanoencapsulation of tannin in order to use these nanoparticles (NPs) in cosmetic products. CS is a natural derived polymer with antimicrobial and antibacterial activity, low toxicity, biocompatibility, and non-allergenicity [3]. CS-NPs are formed spontaneously through ionic interactions between the protonated amino groups of chitosan with the anionic groups of polyanions [4-5]. Hence, Tannin was loaded in NPs of CS in different ratios (10,20 and 30wt%), via the ionic gelation method. Dynamic Light Scattering (DLS) revealed that CS-Tannin NPs had an average size of 189nm. The successful synthesis of CS-Tannin NPs was confirmed by Fourier-transform Infrared (FTIR) while their crystallinity was studied by X-ray Diffraction (XRD), proving their amorphous structure. The resulted CS-Tannin NPs were further utilized for the preparation of innovative O/W cosmetic emulsions. All produced emulsions exhibited good pH and viscosity stability for up to 90 days, while the sun protection factor (SPF) was enhanced due to the presence of the tannin. Additionally, it was found that emulsions with CS-Tannin NPs showed enhanced antioxidant properties due to the phenolic compounds of tannin.

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PICKERING EMULSIONS STABILIZED BY QUERCETIN FOR TOPICAL APPLICATIONS: INFLUENCE OF OIL PROPERTIES

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Emulsions are nowadays widely used in pharmaceutical and cosmetic applications. These systems help encapsulate an active ingredient in a dispersed phase, protect it from degradation, and preserve its activity sustainably. However, they are thermodynamically unstable systems and, thus, require the use of stabilizers in their formulation for long-term stability[1]. Surfactants or polymers are commonly used as stabilizers but raise direct or indirect toxicity and environmental issues. For instance, in long-term topical treatment, skin irritation is often observed[2]. To circumvent toxicity risks, solid particles can be used to stabilize emulsions, referred to as Pickering emulsions. In addition, these emulsions have increased stability compared to conventional ones prepared with surfactants, because the particles are irreversibly anchored at the interface and form an adequate protection against destabilization phenomena such as coalescence[1].

Our work focuses on Pickering emulsions stabilized by quercetin particles. Quercetin is a natural flavonoid compound, found in fruits and vegetables. It exhibits a variety of pharmacological activities such as anti-inflammatory, antioxidant, anticancer, and neuroprotectant[3]. However, if quercetin has recently attracted much attention from dietitians and medicinal chemists, its very low solubility in water limits its oral bioavailability. In a recent study, researchers tested three different approaches to improve quercetin delivery to the skin: liposomes, smartCrystals®, and lipid nanocapsules [4]. The latter two seem promising for quercetin delivery to the upper regions of the stratum corneum and deeper regions of the skin, into viable epidermis. In our project, we used quercetin particles to stabilize Pickering emulsions for topical applications. Thus, the Active Pharmaceutical Ingredient (API) is directly used to stabilize the emulsion. The study aims to investigate the influence of oil properties, especially oil polarity, on the formation and stability of Pickering emulsions stabilized by quercetin particles. Indeed, previous studies have shown that the choice of the oily phase greatly influences on the emulsion formed and its stability [5,6]. Several types of oils of different polarities are chosen as the oil phase to prepare the Pickering emulsions. The stability of the emulsions is characterized macroscopically by microscopy and measurement of droplet diameter.

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ADVANCED RHEOLOGICAL CHARACTERIZATION OF TOPICAL PRODUCTS: AN ACCURATE TOOL TO DISCRIMINATE AND OPTIMIZE FORMULATIONS

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Topical products are widely used to manage skin conditions. Semi-solid dosage forms for therapeutic purpose are known to be diverse: ointments, pastes, gels, bi-gels, foams, lotions and creams. This wide range of textures is due to their complex structure and can be deeply characterized by rheological analysis.
Rheological characterization of formulations is of major interest for two reasons. The first one is to meet the requirements of recently released guidelines by the Food and Drug Administration and the European Medicine Agency, on quality and equivalence of topical products. The characterization of rheological behavior is actively highlighted, as the applicants are highly encouraged to submit a complete rheological profile, addressing rotational and oscillatory measurements [1]. The second one is to understand deeper the microstructure of the different dermocosmetic topical formulations and to put them inperspective with physico-chemical stability data and sensorial analysis. On five creams made of various compositions, a range of well-known rheological critical analytical attributes have been followed through time and at different temperatures. Viscosity, yield point, thixotropic relative area, storage modulus, loss modulus have been measured through different protocols, specifically designed to these products. The results show that rheology is a good tool to discriminate different viscoelastic structures and to detect early instabilities. Rheology assessment has proven to be a useful quality and stability indicator and is a powerful quality control method to ensure that products meet standards and regulations for equivalence of topical generics.

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ALPHA-TOMATINE: A PROMISING NATURAL INGREDIENT FOR SKIN CARE FORMULATIONS

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Green tomatoes, an agro-food industry waste, are rich in the glycoalkaloid alpha-tomatine, which is known to display several health-promoting activities, namely anti-inflammatory, anti-carcinogenic and fungicide, among others. Furthermore, glycoalkaloids are a subgroup of saponins, known foaming and emulsifying agents.[1] This work seeks to establish a sustainable and circular economy process, extracting the tomatine from the unripe tomatoes by subcritical water[2], a state-of-the-art green process, and formulate it into an aqueous foam formulation using alpha-tomatine as both surfactant and active. The extracted tomatine was characterized in terms of its total phenolic compounds, carbohydrates and saponins content. Antioxidant activity was also evaluated by the DPPH (2,2-diphenyl-1-picrylhydrazyl) and CUPRAC (Cupric Reducing Antioxidant Capacity) assays. Anti-inflammatory activity was evaluated in vitro in RAW264.5 cells through the NO production assay. Cell viability in HaCaT cells was also studied. The tomatine containing formulation was prepared using only “green” ingredients. It presented a gel-like appearance and a macroscopic homogeneous foam when using a pump foam dispenser. The foam was evaluated in vitro in HaCaT cells for its cell viability and for anti-inflammatory activity in RAW264.5 cells. The foam viscosity and oscillation were also assessed. Stability of the foam up to 6 months was also evaluated.

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ARE MAKEUP PRODUCTS SOURCES OF PFAS IN EUROPE?

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Per- and polyfluoroalkyl substances (PFAS) are a vaste family of over 4700 chemicals, which have been widely used since the 1940s in industrial processes and many products such as textiles (jackets, carpets,...), building materials, cleansers, polishes, office desks, food contact materials, upholstery, impregnation agents, firefighting foam used to quickly extinguish fire and cosmetic products.**1** In this context, we focused this study on make-up. The qualitative study covered 226 make-up products in 7 categories (lipsticks, nail polishes, eyeshadows, mascaras, BB creams, foundations, face powders). 5 different PFAS have been identified: PTFE, perfluorooctyl triethoxysilane, polyperfluoroethoxymethoxy difluoroethyl peg phosphate, perfluorononyl dimethicone et perfluorononylethyl carboxydecyl lauryl dimethicone. Only 8% of the cosmetics studied contain PFAS. The products containing the most are BB creams, powders and mascaras. None of the 32 nail polish references studied contained PFAS. 4% of the makeup products studied contained PTFE. It is only found in 4 product categories: BB creams, powders, foundations and eyeshadows, which are products applied to the skin of the face and periocular region. 1% of the cosmetics studied contained perfluorooctyl triethoxysilane. Only BB creams (8%) and powders (3%) contain it. 0.4% of the cosmetics studied (1 powder) contained polyperfluoroethoxymethoxy difluoroethyl peg phosphate. 1% of the cosmetics studied (3 mascaras) contained perfluorononyl dimethicone. 0.4% of the cosmetics studied contained (1 mascara) perfluorononylethyl carboxydecyl lauryl dimethicone. It therefore seems that make-up products made in Europe are relatively free from those made in the United States and therefore pose fewer problems than these.

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CERAMIDES AS THE CORNERSTONE IN SIMPLE AND ADVANCED FORMULATIONS TARGETED AT RENEWAL OF DISRUPTED SKIN BARRIER

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Dermatoses are skin diseases caused by lowered level of lipids in the intercellular lipid matrix of skin's uppermost layer stratum corneum. A promising therapy for such cases is the application of liposomally formulated skin lipids (ceramides, cholesterol, fatty acids) that replenish the ones lost due to the skin condition. This work is based on development of ceramide liposomes (cerosomes) that proved highly effective in disrupted skin barrier repair. This unique ability of theirs was also supported by the addition of an anti-inflammatory drug that targets the inflammation often present at the affected sites. The best way of introducing such drug was by the combination of cerosomes with a great topical drug delivery nanovector – lipid nanocapsules (LNCs). LNCs showed great potential in both encapsulating and delivering corticosteroids into the respective cutaneous layers. The fusion of both respective systems ensured not only the mechanical restoration of skin barrier thanks to the ceramides, it also simultaneously effectively delivered anti-inflammatory drugs into the deeper layers of the skin tissue. Moreover, thanks to the uncomplicated preparation process of both nanosystems, this formulation has an exciting potential for the personalization of the product based on the patient's current disease state and prescribed medication.

CHANGES IN SKIN BARRIER PROPERTIES ASSOCIATED WITH EXPOSURE TO SURFACTANT AND ALCOHOL CLEANSERS

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An extensive scientific literature exists on the interaction of surfactant cleansers with the stratum corneum (SC) (1-4). While there remains a robust debate on key aspects of surfactant-skin interactions, the formulation of "mild" surfactant cleansers is now routine. Recent public health concerns have resulted in changes in consumer skin cleansing habits, including an increase in the frequency of skin washing with surfactants and soaps, as well as disinfection with concentrated alcoholic sanitizers. It is reasonable to presume that this change in skin cleansing and sanitizing behavior will compromise skin barrier health via multiple mechanisms. To begin to understand the impact of frequent and repeated cleansing on skin barrier properties, we apply complimentary characterization techniques to measure changes in SC bulk and surface properties, compositional changes, changes in SC barrier function, changes in skin surface topology, and changes in the molecular organizational of the SC lipid lamellae. A range of biophysical techniques including skin wettability via contact angle measurements, attenuated total reflections Fourier transform infrared spectroscopy (ATR-FTIR), scanning election microscopy (SEM), trans-epidermal water loss (TEWL), and chemical analysis are deployed in combination with systematic experimental control of exposure conditions. In a series of initial experiments, we have used the above measurement techniques to characterize ex vivo skin exposed to a harsh surfactant solution (sodium lauryl sulfate) and 85% ethanolic solution. The observed changes in skin surface chemistry and properties indicate that measurable changes to skin surface properties are associated with SLS and ethanol exposure. Rinsing skin after SLS exposure does not remove all the SLS resulting in irreversible changes to the outer SC from bound SLS. Following prolonged ethanol exposure to skin ethanol molecules remain within the SC. SEM images skin exposures to SLS and ethanol show major changes to skin surface morphology. The initial data from this work will be presented along with a discussion of the consequences to skin barrier function and health associated with chronic exposure to surfactant cleansers and ethanolic sanitizers. Once robust experimental protocols have been established this work will be extended to consider the mechanisms and consequences of cleansing damage to skin with inherently compromised barrier function such as atopic dermatitis.

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CONTRIBUTION OF ETHANOL EXTRACTS FROM WHEAT, CORN AND SUNFLOWER WASTE MATERIAL TO THE PROPERTIES AND EFFECTS OF COSMETIC PRODUCTS

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An important contribution to sustainability is research into the usability of ingredients from waste materials (1). Therefore, the aim of our work was to investigate the contribution of ethanol extracts from wheat, corn, and sunflower harvest residues to the physicochemical and applicative characteristics and effects of cosmetic products. With this aim 4 creams were prepared, differing only in the type of extract. Samples without extract and with 0.1% corn, wheat and sunflower ethanol extracts were prepared and labeled P3, CEE, WEE and SEE, respectively. The evaluation was performed by rheology, texture analysis, evaluation of spreadability, stickiness and water washability (2,3). The antimicrobial activity was also investigated. Addition of an extract changed the rheological behavior and parameters such that the creams with extracts were ticker with more pronounced hysteresis area and higher apparent viscosities. Texture analysis showed that after the addition of extracts, the hardness and adhesiveness of P3 changed, but not significantly. Spreadability was similar and slightly increased for all samples with extracts compared to the P3. Stickiness and water washability evaluations were studied with different substrates. The results for stickiness showed a good correlation between the different substrates, while the results for washability could not be correlated. Interestingly, results for WEE were different from the other samples, showing the highest values for stickiness as well as the lowest values for washability. Finally, our antimicrobial activity study showed that all extracts had high to low activity against all microorganisms studied, with the lowest MIC of SEE for S. aureus. Investigated creams SEE and CEE had the same antimicrobial activity against S. aureus and S. epidermidis as P3, suggesting that this activity cannot be attributed to the extract in the cream alone. Nevertheless, the results obtained have given us a new perspective regarding the possible effects and use of extracts in cosmetic products. Our study showed that the investigated waste materials can contribute to the properties and effects of cosmetic products. In this study, the basic formulation was the same for all samples, in order to investigate differences between extracts. Nevertheless, the contribution of each extract will be studied individually by adjusting the composition of the vehicle to support the use of extracts in higher concentration.

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DERMAL COMPATIBILITY AND IMPROVED BARRIER FUNCTION OF A NEW OCTENIDINE AND SILVER CITRATE-BASED EMOLLIENT FOR ATOPIC-PRONE SKIN

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Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases. It usually begins in infancy, although often persists throughout life.1,2 One of the characteristics of AD is a dysfunctional skin barrier, resulting in increased transepidermal water loss (TEWL) and creating a hospitable environment for Staphylococcus aureus colonization,3,4 the density of which correlates with the severity of AD.5 Using moisturisers and emollients as a baseline treatment is strongly recommended in clinical guidelines, including the new clinical guidelines from the American Academy of Dermatology.6,7 We present the results of initial trials done to assess dermal compatibility and the effect on the skin barrier when using a new cosmetic emollient product for atopic-prone skin, containing octenidine and silver citrate as its primary antimicrobial agents. To confirm dermal compatibility, a patch-test trial was carried out on 10 healthy adult participants between the ages of 18 and 70 with sensitive skin. The product was applied to a patch of skin on the back and covered with a protective patch for 48 hours. The results were compared with those from a negative control test (a patch with no product). No participants showed signs of irritation, with the Primary Dermal Irritation Index being 0.00. In paediatric group (between 7 months and 16 years old), the product presented very good acceptability, only one subject (1/20) reported itching of mild intensity lasting a few seconds. Although the paediatricians did not observe any clinical signs of irritation or intolerance, at the end of the study (4 weeks). The effect on the epidermal barrier was examined in 19 healthy volunteers between the ages of 22 and 70, who used the product for four weeks. TEWL was reviewed on days 1 (baseline), 14 and 29. After two weeks of repeat applications, there was a no significant reduction in TEWL when compared to starting values (10.96 ± 0.99 vs. 9.50 ± 0.68; $p \geq 0.10$). However, after four weeks of product use, the reduction in TEWL was statistically significant (10.96 ± 0.99 vs. 7.87 ± 0.41; $p < 0.05$). Finally, 100% of adult patients and 95% of paediatric group reported itching relief thanks to (o after) the application of the product. The results show that this new octenidine and silver citrate-based product, designed especially for those with atopic-prone skin, demonstrated high degree of dermal tolerance, leading to an objective improvement to the skin barrier function.

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EFFECT OF TOPICALLY APPLIED BOLALIPID SURFACTANTS PC-C24-PC AND PC-C32-PC ON CORNEOCYTE COHESION

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Bolalipids represent an interesting new class of surfactants in pharmaceutical technology. Synthetic single chain bolalipids have shown potential as stabilizers for liposome production, and as solubilizing agents for hydrophobic drugs in general [1]. However, the impact of bolalipids on skin barrier function has not been addressed at all so far. In this study, the skin penetration of a hydrophilic permeant, sodium fluorescein, from simple aqueous surfactant dispersions/solutions was investigated using comparative tape stripping on the porcine ear model in combination with NIR-densitometry and fluorescence spectroscopy. Two bolalipid types, PC-C24-PC and PC-C32-PC, were tested against a conventional phospholipid mixture (lipoid S-75), sodium dodecyl sulfate (SDS), polyethylene glycol 12-hydroxystearate (PEG-HS) and water. Results showed that both bolalipids disrupted stratum corneum cohesion when compared to the control treatment with water, resulting in significantly enhanced amounts of removed corneocytes especially on the first tape. Additional experiments with salicylic acid as a reference drug confirmed the observed keratolytic behavior. To gain more insight into potential enhancement effects of different bolalipids on skin penetration of co-applied drugs, in vitro release studies/diffusion cell studies are planned as next step. Ex vivo and in vivo confocal Raman spectroscopy studies will serve to understand the effect of bolalipids on SC physiology.

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EXPLORING A POSSIBLE RELATIONSHIP BETWEEN TRANSEPIDERMAL WATER LOSS AND CERAMIDE LEVELS IN PORCINE STRATUM CORNEUM

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The skin barrier of the stratum corneum (SC) plays a critical role in maintaining skin health by preventing excessive water loss from within the skin as well as protecting against stress factors from the environment [1]. An important part of this barrier is the stratum corneum lipid matrix, which exists as a continuous, lamellar structure throughout the entire SC and is comprised of cholesterol, free fatty acids, and ceramides [2]. Ceramides are the most abundant SC lipid class by weight [3] and changes in the ceramide profile have been observed in skin diseases like psoriasis and atopic dermatitis, which are linked to skin barrier disruption [4]. Impairment of the skin barrier function can be measured using transepidermal water loss (TEWL), which serves as an important indicator of skin barrier integrity [5]. Given the importance of TEWL and ceramides in the context of the skin barrier function, it is reasonable to hypothesize that there may be a relationship between these two parameters, which was investigated in this study. To this end, porcine skin samples were treated with a sodium dodecyl sulfate solution as a skin barrier disruption model, while the control group was treated with pure water. Before and after treatment, TEWL measurements were taken and, after the last TEWL measurement, the SC was separated using trypsin digestion and extracted with a methanol/ethyl acetate mixture for LC-MS analysis of the ceramide content. The results of the measurements were analyzed using multivariate data analysis techniques such as partial least squares and elastic net regression and screened for a potential relationship between the TEWL measurements and the ceramides in the SC. The analysis revealed correlations between ceramide groups as well as single ceramide species and the TEWL measurements representing skin barrier function. Overall, this investigation resulted in the discovery of possible relationships between skin barrier function and certain ceramide species, which could help to improve formulations for skin care and treatments for skin diseases in the future.

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IMPACT OF EMOLLIENTS ON RELEASE STUDIES FROM O/W CREAMS

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The emollient choice of an O/W cream determines its physicochemical properties [1] and, consequently, impacts the release of active substances [2]. This work evaluated the influence of five emollients on the release of hydrophilic and lipophilic drug models from a topical O/W emulsion. The five emollients used (caprylic/capric triglyceride, C13-15 alkane, dicaprylyl ether, dimethicone, and virgin olive oil) differed in structures, molecular weights (from 212.4 to 1522.5), densities (from 0.770 to 0.969 g/mL), and viscosities (from 3.7 to 71.76 mPa·s). Five O/W creams, with 15% of each emollient in a model O/W formulation, were prepared through a standard hot process. Their physicochemical properties were evaluated: pH, droplet size, and "in vitro" release of both models (methylene blue and coumarin) through a hydrophilic synthetic membrane (polysulfone, 0.45 µm) in vertical Franz diffusion cells (n = 3). The results were as follows: pH 4.47 ± 0.10, D50 16.27 ± 8.93 µm, specific surface area 0.87 ± 0.42 m2/g, methylene blue release rate 0.325 ± 0.085 %, and coumarin release rate 1.554 ± 0.818 %. Pearson's linear correlation coefficients, calculated among the properties of emollients and the results obtained from the creams, showed that the density, viscosity, and molecular weight of the emollients favored the release of the hydrophilic model (rd = 0.9375, rV = 0.8393, rMW = 0.1584); conversely, hindered the release of the lipophilic model (rd = -0.8975, rV = -0.5580, rMW = -0.4257). The correlation between the pH and the release rate is higher for the hydrophilic model (rpH = -0.9283) than the lipophilic one (rpH = 0.6701). The droplet parameters, highly and contrarily, affected both release rates: rD50 = 0.9639 and rSSA = -0.9546 for methylene blue; rD50 = -0.9061 and rSSA = 0.9601 for coumarin. All creams presented higher release rates for the lipophilic model (coumarin) than for the hydrophilic one (methylene blue). The release rates are strongly and inversely correlated (rrates = -0.8688), since the parameters of the five emollients and creams that favored the release of the lipophilic model hindered the release of the hydrophilic one. The results of this study indicate that the physicochemical characteristics of emollients influence the release rates of drugs with opposite solubilities, from a model O/W cream.

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NEUTRAL NATURAL DEEP EUTECTIC SOLVENTS AS ANTI-BIOFILM AGENTS IN SKIN FORMULATIONS

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Natural deep eutectic solvents (NADES) are a class of liquids with promising properties as components in pharmaceutical skin formulations, such as a low toxicity profile, biodegradability and versatility. Recently, their potential use as anti-biofilm agents has been proposed, due to their ability to solubilize and stabilize biological macromolecules[1]. A biofilm dispersing or killing effect of NADES would be of great value in anti-microbial preparations for wound and skin infections. In the current work, the ability to break down biofilm matrix and the biofilm killing activity of three NADES of neutral pH were investigated against Staphylococcus aureus ATCC 6538 and Pseudomonas aeruginosa ATCC 9027 biofilms. The tested NADES were choline chloride:xylitol (ChX), choline chloride:glycerol (ChG) and betaine:sucrose (BS). Two of the NADES (ChX and ChG) significantly reduced the number of remaining viable cells of both bacterial species in pre-formed biofilm by 4–6 orders of magnitude, while the average biofilm biomass removal for all NADES was 27–67% (S. aureus) and 34–49% (P.aeruginosa). The tested NADES also inhibited biofilm formation of both bacterial species at concentrations at or below 0.5 x the minimal inhibitory concentration (MIC), possibly in part due to observed restrictions imposed by NADES on planktonic growth. These results demonstrate the potential value of neutral NADES as anti-biofilm agents in future anti-microbial preparations.

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NEW MOLECULES AS SPF BOOSTERS

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Cosmetic products are applied on the human skin and thus they are normally exposed to solar irradiation. Since solar irradiation, in particular ultraviolet radiation, is involved in degradation/aging processes of organic tissue, cosmetic products may include sunscreens, namely molecules capable of absorbing and/or reflecting the radiations. These substances prevent aging of organic tissues by cooperating with the specific cosmetic effect of the product that is being used. The use of sun filters is then the rule in the case of cosmetic products specifically intended for photoprotection, such as for example sun products. Nowadays sun filters are an increasingly discussion topic with regard to their safety for human health[1] and to their environmental impact[2,3]. Besides sun filters, molecules active as photoprotection boosters (SPF boosters) are also known[4,5]: these substances are by themselves generally inactive as photoprotectants, but in the presence of a sun filter are capable of increasing its photoprotective activity. Thus the search for substances with boosting effect is a new prospect in the realization of cosmetic products: this search is in particular directed towards raw materials capable of exerting synergistic effect with both physical and chemical sun filters, thereby allowing the reduction of their concentration in the formula. Then there is a great need of new substances that can be used as SPF boosters, which combine different advantageous properties and in particular: the ease of obtainability and/or synthesis, the feature of being very natural, and a high efficacy that must be as independent as possible on the formulation. This research (under patent protection) is focused on the use of lipo-aminoacid alkyl esters as SPF (Sun Protection Factor) boosters in cosmetics composition comprising a sun filter. These alkyl esters, when added to cosmetic compositions, containing a sun filter, increase their SPF value to an extent of 50% or more. The SPF booster effect was observed in different types of cosmetic formulations and with different sun filters. These alkyl esters have a strong natural connotation, respectful of environment and of the organic tissues, and they can in turn be obtained by an eco-friendly synthesis method which does not involve the use of aggressive reagents, that could remain

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OPTIMIZATION OF ORAC ASSAY COMBINED WITH IN VIVO TAPE STRIPPING FOR THE ASSESSMENT OF ANTIOXIDANT EFFICACY OF COSMETIC FORMULATIONS

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Repeated sun-exposure is one of the main sources of oxidative stress in the skin, which is responsible for the majority of age- ssociated skin conditions. As a result, there has been increased interest in developing novel actives and delivery systems/formulations that effectively inhibit or repair skin damage triggered by UV-induced free radicals. Consequently, there is a need for reliable, cost-effective methods to study their antioxidant efficacy. Therefore, the aim of this study was to optimize a previously developed protocol involving ORAC (Oxygen Radical Absorbance Capacity) assay and tape stripping[1] to investigate skin oxidative state and antioxidative effects of topical treatments in vivo on human volunteers. In this sense, firstly i) the measurement parameters (i.e., fluorescence gain) of the microplate reader (Synergy LX, Multimode Reader, BioTek, USA), ii) the reaction time (between fluorescein and 2,20-azobis(2-methylpropionamidine) dihydrochloride (AAPH) with/without trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) and skin antioxidants) iii) the number of tapes and the protocol for extraction of skin antioxidants, were carefully optimized. Afterwards, the skin was treated with different formulations – i) innovative nanoformulations with/without antioxidants (e.g., French oak fruit extract) and ii) commercially available serums containing vitamin E or vitamin C as controls – to prove the sensitivity of the method. After optimization of experimental conditions (low fluorescence gain, reaction time 120 min, 20 tapes, 10 ml of ethanol for the extraction of skin antioxidants by shaking for 1 h at 200 rpm at 32°C), the intrinsic antioxidant capacity (iAOC) of the intact, untreated human skin (in vivo) was successfully determined. Likewise, the established protocol allowed to detect the oxidative changes in the skin after exposure to different antioxidant formulations/active ingredients. Moreover, the interindividual variability resulted mainly from differences in the amount of stratum corneum removed by tape stripping in the different subjects, implying the need for data normalization for better comparison. Overall, the obtained findings suggest that the ORAC assay in combination with in vivo tape stripping may be a valuable approach to evaluate the antioxidant efficacy of cosmetic formulations, particularly those aimed at neutralizing UV-generated free radicals and preventing harmful sun effects and photoaging of the skin.

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PHYCOCYANIN-ENRICHED COSMETIC GELS: NADES AS STABILITY ENHANCERS?

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Spirulina (Arthrospira platensis) is a renewable source of bioactive compounds interesting for food or cosmetics. In particular, phycocyanin, a phycobiliprotein, is the subject of many studies due to its significant antioxidant activity and blue coloration. Unfortunately, the stability of this molecule in aqueous media is disappointing. Our laboratory previously described the strong potential of Natural Deep Eutectic Solvent (NaDES) to extract and stabilize phycocyanin in a liquid medium, in particular NaDES based on glycerol and glucose1. The objective of the present study is evaluate the impact of incorporating NaDES-based extracts in model gels, to explore the behavior of such complex ingredients in cosmetic formulations. Spirulina extracts were produced from frozen biomass using ultrasonic extraction using a glycerol and glucose-based NaDES. Cosmetic gels based on a semi-synthetic cellulose or a mix of gums were tested. The extracts were introduced at a concentration of 1% and several operating conditions were screened. The stability as well as the colorimetric and antioxidant properties of the gels were observed under accelerated aging conditions (40°C, 75°C humidity, obscurity). The results show that the incorporation of glycerol: glucose NaDES-based extracts in the gels does not significantly modify the pH of the formulations. In contrast, it has a variable impact on the viscosity of the product. On the other hand, phycocyanin color and antioxidant activity can be enhanced, depending on the thickening agent and the process used to prepare the gel. This study highlights the importance of understanding the interactions of NaDES-based extracts with the ingredients of the cosmetic formulation for an effective identification of the best preparation approach.

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SKIN PERMEATION ENHANCEMENT EFFECT BY TARTARIC ACID – MEGLUMINE IONIC LIQUID SYSTEM

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In the past few years, ionic liquids (ILs)—a novel class of environmentally benign and tailor-made solvents—have been increasingly exploited as solvents, co-solvents and/or materials in the fields of pharmaceutical drug delivery and active pharmaceutical ingredient (API) formulation, because of their unique and tunable physicochemical and biological properties. Of particular importance is the application of ILs for pharmaceutical application, —more specifically transdermal drug delivery system[1]. ILs were shown to enhance skin permeation of drugs[1], however, there is a little information available on the ILs composed of high biocompatible materials, pharmaceutical additives, currently used as skin permeation enhancers. We investigated that effect of a novel IL by mixing of tartaric acid (TA) and meglumine (MGM, TA: MGM = 1:2 (mol ratio)) on the skin permeation of isosorbide mononitrate (ISMN) and flurbiprofen (FRP). TA-MGM IL increased the skin permeation flux of ISMN and FRP rather than those in white petrolatum. The flux of ISMN (1.73 ζg/cm2/h) was about 1.4 times higher than that of ISMN in white petrolatum. In contrast, increase the flux of FRP (3.53 μg/cm2 /h) was about 1.3 times than that in white petrolatum. It is suggested that TA-MGM IL would be a candidate of skin permeation enhancer. To elucidate the effect of TA-MGM IL on the intercellular lipids in the stratum corneum (SC), ATR-FTIR stretching peaks TA-MGM IL to hairless mouse skin. The amide I band arises from C=O stretching frequency and the amide II from C-N stretching and N-H bending frequency. The frequencies of these two bands, especially the amide I band, are sensitive and shift to higher or lower frequencies according to changes in SC protein conformation[2]. IR spectra of hairless mouse skin treated with TA-MGM IL revealed significant shift in the amide I and II bands, suggesting that there was alternation of protein conformation in the SC. When considered in the context of skin permeability data, this analysis shows that increased the skin permeation flux correlates with changing SC protein conformation caused by exposure to the TA-MGM IL. In conclusion, the skin permeation of ISMN and FRP increased by TA-MGM IL. This caused that TA-MGM IL alters the SC protein conformation by ATR-FTIR measurements. These results indicate that TA-MGM IL would has a potential tool as a skin permeation enhancer.

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STUDY OF THE POTENTIAL ANTIOXIDANT ACTIVITY OF LUPIN BEANS' BY-PRODUCTS FOR COSMETIC AND PHARMACEUTICAL APPLICATIONS: A GREEN EXTRACTION APPROACH

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In recent years, the circular economy has gained popularity due to its potential to reduce environmental impact and promote economic growth. One way to implement this approach is through upcycling, which transforms waste materials into value-added products [1]. The cosmetic industry is an example of a sector that has invested in designing value-added products with health benefits by using upcycling. Lupin by-products contain significant amounts of health-promoting compounds and have potential health benefits such as antioxidant properties [2]. As lupin beans are an important nutrient source in European diets, this work focuses on studying lupin by-products' bioactive properties and applications using a green chemistry method: extracting lupin bioactive compounds using natural deep eutectic solvent (NaDES) mixtures, ensuring sustainability. Several combinations of NaDES mixtures were estimated by a computational program (COSMO-RS software) [3]. Each mixture's solubility and activity coefficient was predicted to extract bioactive compounds from dry lupin powder. Experimentally, the most appropriate mixtures were proline:glycerol:water (A) and proline:glycerol:sorbitol:water (B), both taking 20 minutes to produce. These mixtures were used to extract bioactive compounds from lupin powder in the solid/liquid ratio of 1:10 for 1 hour at 50oC. Then, the antioxidant activity of the obtained extracts and the respective NaDES mixtures were analyzed using the DPPH assay [4]. The results showed that NaDES mixtures A and B exhibited 69% and 51% inhibition, while their respective extracts showed 75% and 74%. These suggest that NaDES mixtures may enhance the antioxidant activity of lupin extracts. Furthermore, NaDES mixtures can preserve the bioactive compounds and their antioxidant properties from degradation and oxidation, which is a concern with bioactive compounds obtained from lupin extracts. This feature makes these extracts suitable for developing cosmetic and pharmaceutical topical products to protect the skin against the harmful effects of external aggressions at the cellular and structural levels and address skin disorders. Phenolic compounds with potential antioxidant properties can be found in lupin beans, making these extracts versatile and sustainable ingredients for developing innovative products. This approach offers potential health benefits and supports the principles of the circular economy by reducing waste and promoting the use of renewable resources.

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SUSTAINABLE COSMETICS: HARNESSING THE POTENTIAL OF NATURAL DEEP EUTECTIC SOLVENTS FOR CREAM FORMULATION

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Natural deep eutectic solvents (NaDES) are increasingly studied for the preparation of cosmetic ingredients from biomasses as an alternative to conventional solvents. These green ionic liquids are prepared by mixing vegetal cellular constituents and metabolites such as sugars, polyols, or amino acids. Their specific hydrogen-bond network confers high extraction power combined with stabilizing ability, which make NaDES perfect media for sustainable valorization of vegetal biomasses. The resulting extracts are truly biocompatible. Consequently, NaDES-based extracts could be directly included in cosmetic products as the solvent removal step in extraction processes becomes superfluous. It is then necessary to explore the impact of diverse types of NaDES on the stability and the properties of cosmetic products. In the present work, various NaDES compliant to European and Chinese cosmetic regulation were included at 1, 2.5 or 10%wt in creams based on ingredients of natural origins (n=3). Resulting formulations were characterized after 30 days under accelerated aging conditions (40°C, 75% humidity, obscurity). Organoleptic, pH, and rheological analyses were performed to evaluate the impact of the introduction of the NaDES on the stability of the cream. Sensory analyses were also performed on stable samples to evaluate the impact of the introduction of the NaDES for the consumer. Physicochemical studies showed that some NaDES have a significant impact on the product consistency and that this impact is not necessarily proportional to their concentration. Sensory analysis showed that if hydrophobic NaDES in the oil phase have a low impact on the properties of the cream, the inclusion of specific hydrophilic NaDES in the aqueous phase could have a positive impact on the sensory properties. This study indicates that if some NaDES do not show appropriate formulability, several NaDES could be used to prepare vegetal extracts that can be introduced up to 10% in the oil or aqueous phase of creams. Moreover, the introduction of specific NaDES improved the properties of the model formulations. The results of this study are definitely in favour of the development of the exploration of NaDES as sustainable cosmetic ingredients.

THERMAL WATER COMBINED WITH THYMUS X CITRIODORUS HYDROLATE AS CORE INGREDIENTS OF ANTI-AGING COSMETIC PRODUCTS

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Skin-aging is a natural process with loss of structural integrity and physiological function mostly due to reactive oxygen species activities. Recent trends in anti-aging research and marketing sustain the use of natural resources as core ingredients for cosmetic products. Portuguese thermal waters and Thymus x citriodorus hydrolate (by-product of essential oil) have proven their potential as cosmetic ingredients with hydrating, anti-oxidant and anti-inflammatory activities that may decrease skin aging signs. To develop a natural anti-aging day cream that combines a Portuguese Thermal Water and Thymus x citriodorus hydrolate as core ingredients. The principles for the development of this cream involved criteria of minimalism, degree of naturalness and sustainability. Additionally, the ingredients were selected based on their anti-aging, lifting, and hydration claims. Core active ingredients were selected based on information from the literature and on previous in vitro studies from our research group on thermal waters and Thymus x citriodorus hydrolate. Other commercial ingredients were selected based on the documentation made available by the suppliers. These included humectants (Glycerin) to mimic the natural moisturizing factor, moisturizers (Allantoin), emollients (Grape Seed Oil), antioxidants (Vitamin E), fatty esters of vegetable origin (Capric/Caprylic Triglycerides) and actives that repair the skin barrier (Niacinamide).. The day cream was prepared at low temperatures, pH value was adjusted to 5 respecting the skin physiology. Stress onditions were tested through centrifugation for thirty minutes at 3000 rpm. For rheological characterization, a cone-plate viscometer was used, and measurements were performed under controlled temperature conditions (T=25 °C ± 2 °C) for 1 minute. Further stability testing was assessed through temperature cycling (4 weeks).. We have developed a moisturizing day cream with an emollient and anti-aging composition with an advanced texture. Viscosity of the day cream was identified as a key parameter for performance. Through rheological characterization it was classified as a non-newtonian, shear thinning fluid (for shear rate values of 20, 40, 60, 80, 60, 40, 20 (1/s) we obtained viscosities of 7630, 3934, 2762, 2175, 2699, 3711, 6489 (cP) respectively) with thixotropic behavior (positive hysteresis area). Safety of the formulation is further supported by safety assessment calculations, according to the EC Regulation no 1223/2009 based on each ingredient selected for this formula. The formulation of the day cream with two endogenous Portuguese products (Thermal Water and Thymus x citriodorus hydrolate) was successfully completed. Textural and stability to centrifuge testing properties support further stability assessment, in vitro and in vivo testing of these products.

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WASTE MATERIALS FROM WHEAT, CORN AND SUNFLOWER IN COSMETIC PRODUCTS

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Due to sustainability requirements, a particular interest is focused on cosmetic ingredients derived from plant waste materials (1). The aim of our work was to investigate the potential of different extracts from wheat, corn and sunflower waste material for the development of stable cosmetic creams. After the development of placebo formulations, lipid and ethanol extracts from corn, wheat and sunflower were used to prepare 12 creams. Formulations containing 2% and 10% lipid extracts and 1% and 0.1% ethanol extract were prepared. In our preliminary study, the prepared creams were characterized by rheological measurements, pH, conductivity and organoleptic properties. Creams containing 2% lipid extracts were soft creams, differing significantly in color, odor and physical appearance. Creams with 10% of lipid extracts showed immediate instability or instability after 2-3 weeks. Although our study confirmed that stable creams can be formulated with 1% ethanol extracts, it was evident that certain sensory properties (appearance, color, and odor) of these creams might be unsatisfactory to an average consumer. In this context, 3 creams containing 0.1% ethanol extracts were prepared and characterized. After incorporating each extract into the placebo formulation, the pH was slightly lowered. The conductivity and especially the emulsion type changed from the mixed emulsion of the placebo cream to oil-in-water emulsions. This indicates that the addition of the extracts affects the microstructure of the emulsions. This was confirmed by rheological measurements. It was showed that the addition of an extract resulted in changes in rheological behavior and parameters (hysteresis area, minimal and maximal apparent viscosity). Our preliminary study showed that the investigated waste materials can be incorporated into cosmetic cream formulations. However, extracts must be used at certain concentrations to obtain stable products. In general, the concentration of each extract must be studied on a case-by-case basis. Even though stable cosmetic products can be made with the ingredients studied, in order to develop a product that is acceptable and appealing to the consumer, the formulator must be experienced in cosmetic formulation development, and each ingredient must be carefully selected for compatibility between the ingredients and the general product properties.

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3D PRINTING: NEW DIRECTIONS TO PERSONALIZE THE DELIVERY OF (BIO)ACTIVES FROM TOPICAL PATCHES

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3D Printing (3DP) is a cutting-edge technology that provides a spatially controlled method for producing personalized topical patches with different compounds, dosages, geometries (shape and size), and release rates. Given this scenario, 3DP offers the necessary versatility to quickly modify and adjust the patches to the to the consumer's features and needs, which represents a market trend [1]. This research aimed to study the influence of patches' internal design in releasing kinetics and permeation profiles of 3D-printed patches for topical delivery of Niacinamide, using in vitro and in vivo approaches. 3-layered gelatin-based patches containing RonaCare® Nicotinamide as an anti-aging cosmetic bioactive (INCI: Niacinamide, Merck KGaA, Darmstadt, Germany) were printed by an extrusion-based 3D-printer (Allevi2, Allevi, USA). Prior to printing, the design of the patches was personalized using the Allevi2 Online Slicer, varying the infill type (IT, Grid vs Triangular) and infill distance (ID, 1.3-0.7 mm) settings. The patches' topography was examined using Visioscan® VC 98 (Courage + Khazaka electronic GmbH, Cologne, Germany). The in vitro release assay (n = 6) was performed according to [2], and the absorbances were measured in a Fluostar Omega microplate reader (BMG Labetch, Germany). For in vivo penetration studies, (n = 10 volunteers; 3D-printed patches applied under occlusion for 24 hours), a Confocal Raman spectroscopy (CRS) was used (gen2-SCA, RiverD, Netherlands), recording at a maximum depth of 40 µm. In vitro, triangular-design patches showed a similar release kinetics, with an initial bursting effect followed by a controlled release mechanism; however, the variation of the ID from 0.7 to 1.3 mm seemed to accelerate the release rate. The influence of IT was also observed, with the grid-design patches showing slower release kinetics than the triangular patches. Other relevant studies are ongoing to: i) quantify the in vivo skin penetration of Niacinamide based on CRS; and, ii) explore the possibility of incorporating different concentrations of Niacinamide within the same patch structure according to the skin location needs. Overall, this work delivered insight into the practicality of using 3DP to personalize the bioactives' release by employing straightforward construction design strategies. In addition, new directions for evaluating and adjusting cosmetic outcomes can be explored though the possibility of quantifying such effects in vivo.

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A COMBINED APPROACH TO BETTER UNDERSTAND THE ABSORPTION PERCEPTION OF SKINCARE PRODUCTS

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Consumer expectation is an important aspect of the cosmetic formulation process. When an expectation is not attended to, disappointment can arise and compromise a product's acceptance. Therefore, it becomes essential to consider consumers' opinions and expectations on the development process of new formulations [1]. To do this properly, sensory analysis is a key element, as it searches to better understand consumers' perceptions and materializes them into concrete data that can be further explored and used[2,3] prior to placing a cosmetic product on the market. In sensory evaluation, it is not always an easy task when we consider inter-individual differences, such as skin type[4]. Going further on this topic, here the aim was to better understand what kind of role skin type plays when it comes to product absorption. For that, a panel of 33 volunteers, with different types of skin, according to biometrological measurements (corneometry and TEWL) were recruited. A combined sensory and instrumental approach was developed and applied to better understand the phenomenon of absorption of different skincare products. The sensory evaluation of the absorption was evaluated according to a strict protocol by the volunteer first, then by the operator using the same protocol in a blind manner and thirdly instrumentally using a method developed in the laboratory using the frictiometer and being highly correlated with sensory data[6]. This study is of great interest in the cosmetic field, it helps to better understand the phenomenon of absorption of different skincare products and therefore to adapt efficiently the methods of sensory analysis.

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APPLICATION OF PHYSIOLOGICALLY BASED PHARMACOKINETIC MODELLING TO PREDICT THE IN VITRO DERMAL PERMEATION OF THE UV FILTER OCTOCRYLENE

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Dermal physiologically based pharmacokinetic (PBPK) models have garnered increasing attention in both medical and personal care industries in recent years. PBPK models incorporate information on human skin physiology, dynamic formulation characteristics and trial design to mechanistically simulate skin absorption [1]. UV filters are active ingredients in sunscreen products which can protect the skin from UV radiation. In 2019, the US FDA proposed new regulations for sunscreens, requesting additional safety data such as dermal absorption data for 12 commonly used UV filters, including octocrylene [2]. The present study demonstrates that a properly parameterized dermal PBPK model can be utilized to predict in vitro skin permeation and skin retention of UV filters from commercial sunscreen products with various formulation designs under different experimental conditions. The Simcyp simulator's Multi-Phase Multi-Layer (MPML) MechDermA model[3] was utilized to simulate the in vitro skin permeation of octocrylene from commercial spray, lotion and cream formulations through dermatomed skin and heat separated human epidermis, published by Yang et al. in 2020 and 2022 [4, 5]. The physicochemical properties of octocrylene were sourced from the literature. The reported [4, 5] globule size of dispersed phase was used to parameterize the lotion and cream formulation models. To simulate the alcohol-based spray formulation, the solvent evaporation rate was predicted using the vapor pressure of ethanol. The in vitro permeation test (IVPT) trial design, including dosing regimen, skin membrane type, and receptor medium composition, were informed by the published studies [4, 5]. The partition and diffusion coefficients through/in different skin layers were predicted using QSARs built into the Simcyp MPML MechDermA model. The stratum corneum lipid:vehicle and receptor:membrane partition coefficients were optimized and verified by simulations of independent permeation data . Simulation results were compared to each donor's observed data by calculating the predicted to observed ratios (P/O ratio). Sensitivity analysis was performed on various formulation characteristics, such as evaporation rate, solubility, droplet size and viscosity, to determine their effects on predicted skin permeation of octocrylene. The model accurately captured the skin permeation profiles of octocrylene from the assessed formulations in both dermatomed and heat separated human skin, under both finite and infinite dose conditions, with the majority of individual data falling within the 95th and 5th percentile of the simulations. P/O ratios of maximum cumulative amount through dermatomed skin were 0.09 to 1.64 (4 donors), 0.84 to 2.46 (2 donors) and 0.11 to 6.57 (4 donors) for the lotion, spray and cream, respectively. For the permeation through epidermis, the P/O ratios were 0.75 to 2.24 (3 donors) and 2.01 (1 donor) for lotion and cream under finite dose. The cream was not investigated under infinite dose conditions. The P/O ratios were 1.41 and 1.13 for the single donor data reported for the lotion and spray, respectively. The simulated skin retention was also compared to observed data. For epidermis IVPT studies, skin retention was only reported for finite dose experiments. A good prediction was obtained for the lotion formulation with P/O ratios from 0.76 to 1.10 (3 donors) and 0.57 to 1.95 (3 donors) for dermatomed and epidermal membranes, respectively. Furthermore, the model accurately captured the skin retention of the cream formulation in dermatomed skin (P/O ratios from 0.86 to 2.11, 3 donors), while over-

predicting the retention in epidermis (P/O = 6.27, 1 donor). Since the observed skin retention was reported for a single donor, it is unclear whether this individual is representative of the population or lies outside the simulated 95th and 5th percentiles. For the spray formulation through epidermis under finite dose conditions, a low mass balance recovery was reported , making comparison to simulations unreliable. Additionally, the results of sensitivity analysis revealed that formulation characteristics, including solubilities, vehicle evaporation rate, and droplet sizes, are sensitive parameters that can significantly affect the skin permeation and retention of octocrylene to varying degrees. Conversely, other characteristics, such as viscosity, were found to have minimal impact on the dermal absorption.

To the best of our knowledge, this is the first study using a dermal PBPK model to predict the in vitro skin permeation of a UV filter from commercial sunscreen formulations. This model can be a valuable tool for making informed decisions during the product development process. Our study also highlights the utility of PBPK modelling in the safety assessment of sunscreen products and as a tool for selecting formulations to be used in maximal usage clinical trials.

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BIOPRINTING TECHNOLOGY TO BUILD A NEW EQUIVALENT SKIN MODEL WITH SEBACEOUS GLAND-LIKE STRUCTURES

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Sebaceous glands are holocrine glands that secrete sebum on the skin surface. Sebum plays a role in hydration, thermoregulation, and microbial protection. Currently 3D models with sebaceous glands consist of skin explants, sebaceous gland explants or 3D skin organoids. Skin explants and isolated sebaceous glands are difficult to procure, hard to cultivate, provide only a limited number of samples, and present donor-donor heterogeneity. There is therefore a need to generate bio-engineered 3D skin models containing sebaceous gland-like structures. Bioprinting has become an essential tool in skin bio-engineering. Bioprinting technologies can be grouped in nozzle-based and nozzle-free technologies. For this study we used a hybrid bioprinter combining both technologies. We first set up sebocyte bioprinting parameters using an affordable and easy to cultivate rodent sebaceous cell line, before switching on a human sebocyte derived from hiPSCs (human induced Pluripotent Stem Cells). After generating spheroids by printing spots of rodent sebocytes on a collagen layer, we switched to hiPSC-derived sebocytes which generated viable aggregates of 150µm of diameter. When treated with compounds inducing terminal differentiation, markers such as FASN (Fatty Acid Synthase), PLIN2 (Perilipin-2) and accumulated lipid droplets were increased. Finally, sebaceous structures were included into full skin models. Our model adds to the 2 existing bio-engineered skin models containing hiPSC-derived sebocytes. We are hoping to use it in evaluation of compounds acting in multicellular level. Further studies will focus on improving our full-skin model and testing inhibitors and other inductors of sebocyte maturation.

CHARACTERIZATION OF KNEE AGING BY FRINGES PROJECTION, STANDARDIZED PICTURES AND VISCOELASTIC METHODS

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Skin aging and its quantification is very well known on face, however, other sites are also very visible, and the knee is one of them. With aging the knees become dryer, more wrinkled and can suffer of ptosis. UV exposure as well as specific life conditions can also promote knees wrinkles. This problem can be very impactant for people in their social relation and self-esteem. Metrological evaluation of knees wrinkles is not an intense field of research and few publications are presenting standardized methods. Our aim was to set up illustrative and quantitative methods capable of showing knees wrinkles changes thru aging. The difficulty to acquire such a moving part of the body with standing volunteers obliged us to develop 2 specific methods. First method consisted in a standardized acquisition with a photographic bench. Second method consisted in performing 3D acquisition by Fringes Projection (AEVA). Moreover, we tested existing devices for skin visco-elasticity and density (ElastiMeter, Cutometer® and Ultrasound DermaScan® C). 30 female volunteers aged 21y to 71y (mean 51y) and with Body Mass Index between 18 and 24 were recruited and submitted to various measures and acquisitions on the upper and middle part of right and left knees. For each method, the panel was divided into 3 age groups (young, middle, and old) and the correlation between calculated parameters and age was evaluated. The photographic bench and the fringes projection bench were both set up to achieve a good contention of volunteers and allowed us to build up a pictures and 3D atlas with six age categories (20-30-40-50-60-70 years old). Moreover, with the fringe's projection analysis, we performed various calculation on roughness parameters (Ra, Rq, Rz) or density. All our parameters showed a positive correlation with age and the three age group were significantly different. Regarding elasticity with the Cutometer®, all the parameters (R ,F or Q parameters) were tested and all showed a high correlation with age and a significant split of three age groups. We have confirmed that wrinkles and elasticity on the knee are age dependant. Moreover, amongst various quantification methods, we found that fringes projection and Cutometer® parameters are the best to precisely quantify knee aging. The standardized 2D and 3D pictures provided by our benches are interesting for illustrative purpose and comparison over the time.

DERMATOLOGICAL ANALYSIS OF ALLERGIC CONTACT DERMATITIS AND PSORIASIFORM DERMATITIS IN MOUSE MODELS

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Contact hypersensitivity (CHS) is an experimental model of allergic contact dermatitis (ACD) that can be studied in mice. To induce CHS, mice are sensitized and 4 days later again exposed (elicitation, challenge) to a hapten such as 2,4,6-trinitrochlorobenzene (TNCB). This model represents an objective laboratory method that may help to understand the CHS reaction in mice, and this can be measured and quantified by various parameters. Many autoimmune disorders such as psoriasis lead to the alteration of skin components which generally manifests as unwanted topical symptoms. One of the most widely approved psoriasis-like animal models is the imiquimod (IMQ)-induced mouse model. This assay mimics various aspects of the complex cutaneous pathology and could be appropriate for testing topical treatment options. In the current study preclinical mouse models of ACD and psoriasis were analyzed by the evaluation of the changes in skin thickness (swelling), skin morphology (scanning electron microscopy) skin histology (H&E staning), skin composition (by confocal Raman spectroscopy), skin permeability (in dynamic diffusion cells), barrier function (TEWL) and inflammatory biomarkers (cytokine ELISA plate array) in control and diseased animals. The results indicate that TNCB-induced ACD can recapitulate the human disorder by showing the measurable consequences of T cell-mediated immune response (swelling, morphological changes in inflamed tissue, the release of proinflammatory cytokines – leptin, IL-1a, SCF, G-CSF, IL-4, resistin - increased water content and reduced ceramide and lactate composition in the epidermis, impaired barrier function, and enhanced permeability. The IMQ-induced psoriasis model also successfully produced the main symptoms of the human disease such as scaly stratum corneum, raising levels of inflammatory cytokines – IL-17a, IL-2, IL-4, leptin, VEGF, GM-CSF, IL-1b, Mip-1a -, which peaked at 24h after the induction, deteriorating barrier function and also increased permeability for the topical model drug. These results indicate that both preclinical models can be utilized for testing topical medicinal products and different formulations against ACD or psoriasis and are also appropriate tools for the evaluation of the dermal pathology processes during disease development. For identification of molecular therapeutic targets genetically modified mouse models are under development.

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HYDROGEL-FORMING MICRONEEDLES WITH SOLID DISPERSION RESERVOIRS FOR THE LONG-ACTING TRANSDERMAL DELIVERY OF ATORVASTATIN

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Using hydrogel-forming microarray patches (HF-MAPs) facilitates the delivery of numerous hydrophilic molecules transdermally without harming the skin. This is driven by the HF-MAPs' hydrophilic properties[1]. However, a large fraction of drugs in clinical trials and on the market are lipophilic drugs requiring relatively high doses[2]. This study proves, for the first time, the feasibility of transdermal long-acting atorvastatin (ATR) delivery using HF-MAPs in conjunction with poly(ethylene)glycol (PEG) solid dispersion (SD) reservoirs. This cutting-edge technology offers a potential long-acting, less intrusive alternative delivery mechanism that could enhance patient compliance and treatment results. HF-MAPs were prepared by casting hydrogel blends containing 20% w/w Gantrez S-97 (a copolymer of methylvinylether and maleic acid (PMVE/MA)), 7.5% PEG 10,000 and 3% sodium carbonate in moulds containing 19x19 conical shaped needles cavities (391 needles). They were centrifuged at 3500 rpm for 20 min, left to dry at room temperature for 48h, then crosslinked for 24h at 800C. ATR-SD reservoirs were made by dissolving ATR in PEG 200, then mixing it with PEG 6000 in a ratio of 3:1. The mixture was vortexed and placed at 800C for 15 min until completely dissolved. Then 0.25g were cast in 1 cm2 square silicone moulds and left to dry for 5 min. Franz-cells were used to study the ex vivo permeation of ATR through HF-MAPs. Sprague Dawley rats were used for the in vivo study, taking place over two weeks. Each rat received 4 HF-MAPs, each with an ATR reservoir (60 mg of ATR in total), compared to oral group receiving 10 mg/rat. Franz cells ex vivo permeation profiles revealed that after 24 hours, 2.05±0.23 mg of ATR was delivered to the receiver compartment. The in vivo study showed that ATR was delivered over the study duration of two weeks following a single dose administration. This is the first time to demonstrate the versatility of HF-MAPs in the long-acting delivery of a hydrophobicdrug. Therapeutic levels of ATR were detected and quantified in the rats' plasma throughout the study. HF-MAPs with PEG SD matrix could enhance the transdermal delivery of ATR, as compared to control setups. Ex-vivo permeation tests revealed that the PEG reservoirs successfully delivered ATR through porcine skin via HF-MAPs. The in vivo study proved the ability of HF-MAPs with SD PEG reservoirs to achieve sustained ATR delivery over two weeks.

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IN VITRO PERMEATION TESTING: ASSESSMENT OF SAMPLING TECHNIQUES AND ANALYTICAL METHODS

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The FDA published a draft guidance on establishing topical formulation bioequivalence with in vitro permeation test (IVPT). Receptor fluid sampling has historically used the aliquoting technique for static diffusion cells. However, the draft guidance advises full volume replacement for the purposes of maintaining sink conditions and avoiding negative flux. The objectives of the experiment were to determine if there were differences between these two receptor fluid sampling techniques using Teledyne Hanson Phoenix DB6 static diffusion cells, and whether analytical sensitivity influenced the profiles that the sampling techniques generated. Formulations containing Diclofenac sodium (1%, w/w) or [14C]-Testosterone (0.1%, w/w) were prepared in propylene glycol: water (80:20, v/v) and applied to skin samples mounted in cells set to maintain a skin surface temperature of 32 ± 1°C. Absorption was assessed by sampling at timepoints over a 48 h period for Diclofenac sodium and over a 24 h period for [14C]-Testosterone. For aliquoting, a single 250 µL aliquot was taken using a positive displacement pipette. For full replacement, the entire contents were removed by pouring the contents from the cell. Pre-warmed receptor fluid was used to replenish the receptor chamber volume after each timepoint (except the terminal timepoint) for both sampling techniques. Receptor fluid samples were analysed by liquid chromatography with tandem mass spectrometry (Diclofenac sodium) or liquid scintillation counting ([14C]-Testosterone). No clear differences could be observed in the cumulative absorption (AMT) and flux profiles for Diclofenac sodium (AMT = 8439 ± 3391 ng/cm2 (aliquoting) and 8983 ± 4195 ng/cm2 (full replacement); Jmax = 506 ± 299 ng/cm2/h (aliquoting) and 562 ± 275 ng/cm2/h (full replacement) at 30 h post dose) and also for [14C]-Testosterone (AMT = 2862 ± 2019 ng/cm2 (aliquoting) and 3125 ± 2340 ng/cm2 (full replacement); maximum flux = 222 ± 158 ng/cm2/h (aliquoting) and 228 ± 164 ng/cm2/h (full replacement) at 24 h post dose). The experiments confirmed comparable profiles could be generated using both aliquoting and full replacement technique with the Teledyne Hanson Phoenix DB6 static diffusion cells, and that both analytical methods are robust enough to analyse samples obtained by either sampling technique.

INVESTIGATION OF THE SUITABILITY OF CONFOCAL RAMAN SPECTROSCOPY FOR THE DEMONSTRATION OF BIOEQUIVALENCE OF TOPICAL PRODUCTS

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Based on the EMA draft guideline on quality and equivalence of topical products and the EMA guideline on the investigation of bioequivalence, when investigating skin penetration, bioequivalence is defined as the penetrated amount of the comparator drug being within a confidence interval of 80 - 125 % of the reference drug [1, 2]. When evaluating the bioequivalence of different drugs in terms of skin penetration, tape stripping is currently the most widely used method [3-5]. Since tape stripping is a destructive method, the aim of this project was to demonstrate the suitability of the non-destructive method of confocal Raman spectroscopy (CRS) for determining the bioequivalence of topical products. Ketoprofen was used as a model active, with Effekton gel as an on-the-market drug product. Effekton was tested against itself to obtain bioequivalence. To generate a model formulation that is not bioequivalent, Effekton was diluted 1:2 with carbomer gel. The incubation times used amounted to 15 h with formulation on the skin (invasion phase) and, in a second set-up, a further 6 h of incubation after the formulation was removed from the skin (depletion phase). CRS measurements were performed using a NIR laser with a wavelength of 785 nm. Ketoprofen concentration was measured up to 50 µm into the skin with a spectrum taken every µm and an accumulation time of 3 sec. Additionally, tape strips were taken from the skin and extracted with methanol in an ultrasonic bath after peeling off [6, 7]. Then, the ketoprofen concentration was quantified by HPLC [8]. In order to show a direct correlation between tape stripping and CRS, both experiments were performed consecutively on the same skin samples. Results show that there is a correlation between the two methods.

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LOW FIELD NMR METHODS TO EVALUATE THE HYDRATION STATE OF SKIN EXPLANTS

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The evaluation of the hydration efficacy of active ingredients or finished product formulas remains a major challenge for manufacturers before moving on to the clinical trial stage. In this context, the objective of the project is to develop an original and innovative approach using NMR (Nuclear Magnetic Resonance) methods to measure hydration in ex vivo models such as skin explants, but also to characterise the compartmentalisation of water within the tissue (tightly bound water/bound water/very free water). In this context, the development of an experimental protocol adapted to the study of skin explants, the development of NMR sequences and calculation methods have led to a method for measuring the hydrating efficacy of isolated active ingredients or finished product formulas. Low field NMR analyses are performed on a Bruker Minispec NMR machine operating at 20 MHz. Different NMR analyses are performed to measure:

- the water content of the explant,
- the binding forces of water within the tissue,
- the compartmentalisation of the water (tightly bound water/bound water/very free water).

These measurements are performed on each explant before and after application of the isolated active ingredient or finished product formula to be tested. Compared to an untreated control, the moisturising efficacy can thus be measured after a defined post-application time and possibly be followed over time with longer kinetics.

MICROFLUIDIC MANUFACTURE OF HIGHLY LOADED MELATONIN SNEDDS USING 3D PRINTED CHIPS FOR TREATMENT OF VESICANT CHEMICAL WARFARE AGENTS

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Melatonin is an indoleamine used commonly for sleeping disorders at low doses. Melatonin has been shown recently to modulate the inflammatory response, neutralize oxidative stress and prevent DNA damage [1]. Topical commercial formulations are available with concentrations ranging up to 1% w/w for skin anti-aging purposes. Vesicant chemical warfare agents induce oxidative damage and cellular macromolecule alkylation, which melatonin can counteract if available at higher concentrations [2,3]. Previous studies used lipid-based formulations with ethanol to solubilize melatonin in high concentrations [2]. This project aimed to optimize topically highly concentrated melatonin scalable delivery systems that are able to minimize oxidative damage and alkylation of the cellular macromolecules and enhance cutaneous regeneration. In this respect, we developed highly loaded (5%w/w) self-nano emulsifying drug delivery systems (SNEDDS) with known high skin permeability based on GRAS low irritation excipients and without the use of irritant solvents as permeability enhancers (ethanol, transcutol). Resulting SNEDDS are isotropic mixtures of oil and surfactants, which are also likely to increase melatonin stability and shelf-life as aqueous systems are prone to oxidation. Both conventional and microfluidic manufacture using a 3D printed X-shape microfluidic chip will be employed. As a proof of concept, both the conventional method to prepare SNEDDS that requires 24-48 h stirring to reach solubility equilibrium will be compared with a more intensified mixing to significantly decrease the preparation time using 3D printed microfluidic chips for the first time [5]. Solubility studies were performed in oils, surfactants, and cosurfactants [3]. Pseudo-ternary phase diagrams were carried out to evaluate the optimal formulation yielding a Type II microemulsion. A D-Optimal design was developed using different mixtures of Labrasol, Capryol 90, and Labrafac Lipophile WL 1349 using the Design Expert 12 software (State Ease, Minneapolis, MN, USA). Diffusion studies of optimized melatonin-loaded SNEDDS (5% w/w) were performed using vertical diffusion Franz Cells (Soham Scientific, Loughborough, UK) as previously described [4, 5]. Melatonin concentration was quantified using a validated HPLC method previously developed (Jasco Inc., Maryland, USA) [6]. The microfluidic chip was designed using Solidworks® (Autodesk®, Mill Valley, CA, USA) and printed using the Anycubic® Photon Mono X SLA printer and photopolymerization of the Anycubic® UV sensitive resin at 405 nm (Figure 1). To continuous manufacture SNEDDS using microfluidic chips, melatonin dissolved in Labrasol was flown at 0.5 ml/min via one inlet port. At the same time, a mixture of the cosurfactant (Capryol 90) and oil (Labrafac) were pumped via the second inlet at the same flow rate. The final product was collected and diluted 1/1000 v/v with deionized water for particle size analysis distribution and morphology analysis at transmission electron microscopy (TEM) to compare the particle formation between the conventional and microfluidic methods. Melatonin showed a significantly higher solubility in Labrasol followed by Capryol 90 and Labrafil M 1944 CS, and these excipients were selected as surfactants, cosurfactants, and oily phase for the pseudo-ternary diagrams. The optimal excipient combination was calculated by targeting a 100 nm particle size upon dilution and the highest drug loading. Optimal SNEDDS composition

consisted of Labrasol: Capryol 90: Labrafac lipophile WL 1349 in the ratio 49:33:18 w/w. The optimized melatonin-loaded SNEDDS exhibited a particle size upon dilution of 102 ± 3 nm and 5% drug loading. Optimized melatonin-loaded SNEDDS showed a high steady-state transdermal flux, 169 µg/cm2/h (Fig. 2), with a 15 min lag time. The low viscosity of SNEDDS allows easy spreadability in large areas of skin if necessary. Microfluidic manufacture enabled the manufacture of SNEDDS with similar particle size and morphology but allow a reduction of manufacturing time to less than 1 minute. Optimized melatonin SNEDDS possess high topical permeability making them a promising approach for acute treatment of exposures to VCWs to prevent or reduce skin lesions. 3D printed microfluidic chips have been successfully applied in manufacturing melatonin SNEDDS leading to a significant reduction in time preparation compared to conventional manufacturing methods.

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OPTIMIZATION OF IONTOPHORESIS PROTOCOL FOR THE SKIN PENETRATION OF A CHARGED HYDROPHILIC COSMETIC ACTIVE EFFECTS

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The effectiveness of cosmetic products relies on the skin penetration of active molecules to specific target areas. Iontophoresis may enhance the transdermal administration of charged molecules since it utilizes the combined effects of electro-repulsion and electroosmosis between two electrodes applied to the skin1. When an electric current is applied, a negatively charged active molecule located at the cathode is repelled into the skin towards the anode. Simultaneously, Na+ ions present in the skin migrate towards the cathode, creating a solvent flow through electroosmosis2. The aim of this study is to investigate the bipolar iontophoresis as a promoting technique for the skin penetration of an anti-ageing molecule as a stabilized ascorbic acid derivative produced from Vitamin C and starch (AA2G). For this purpose, a Franz diffusion cell was used. This system consists of a donor compartment, where the formulation containing the active molecule is applied to the skin surface, and an acceptor medium that simulates blood. Pig skin explants were placed between these compartments to mimick human skin. Electrodes were applied to the explant surface for the iontophoresis treatment. The amount of AA2G present in each skin layer (stratum corneum, viable epidermis and dermis) was subsequently determined by Ultra Performance Liquid Chromatography. A screening design was used to study the effect on AA2G skin penetration of the current intensity and the formulation deposit considering the location of the electrodes. The results were compared to the passive diffusion of AA2G through the skin. A significant improvement of AA2G skin penetration was observed by using iontophoresis under specific operating conditions. Intermediate current intensities were required to increase AA2G concentration in the skin layers. We also varied the way to depose AA2G onto the skin: with or without contact between electrodes through the formulation, by applying AA2G formulation under both electrodes or not. The deposit conditions showed important influence on AA2G skin penetration. Results indicated that the negatively charged AA2G molecule may be effectively electro-repelled into the skin from the cathode towards the anode, despite the occurrence of electroosmotic flow in the opposite direction. The performed experimentation allowed determining the optimal operating conditions required by the iontophoresis technique to significantly improve the skin penetration of AA2G.

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PROGRESS IN THERMODYNAMIC MODELLING OF FORMULATION EFFECT ON PERCUTANEOUS ABSORPTION

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A wide range of product formulations have been used for skincare products and dermatological drugs. Examples include creams, ointments, emulsions, and dispersions, to name a few. Understanding how different product formulations affect percutaneous absorption is critically important for delivering human skin care and health, but studies on the subject are very limited. We present progress in developing a thermodynamic modeling approach to predict formulation impact on transdermal permeation. First, by applying interfacial mass transfer equation, we show that the diffusion and partition properties of functional ingredients in both product formulation and skin substrate are critical parameters affecting percutaneous absorption[1]. Molecular dynamics modeling combined with quantum chemistry modelling are then applied for ab initio simulation of solute partition in complex formulations as well as in skin substrate. In particular, solute partition of a wide range of solutes in surfactant micelles and oil water emulations are predicted. The predicted results are in good agreement with experimental data[2, 3]. Molecular dynamics and quantum chemistry modelling have been also conducted to elucidate how dermal exposure to skin care and dermatological drug ingredients such as glycerol and ethanol affects the integrity and solute partition property of stratum corneum lipid barrier[4]. Finally, we present examples of how molecular dynamics modelling can be combined with physiologically based pharmacokinetics modelling for a fully integrative end-to-end thermodynamic modelling of formulation impact on percutaneous absorption.

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TACTILE SENSORY EVALUATION: AN ESSENTIAL TOOL TO EVALUATE SKIN-PRODUCT INTERACTION

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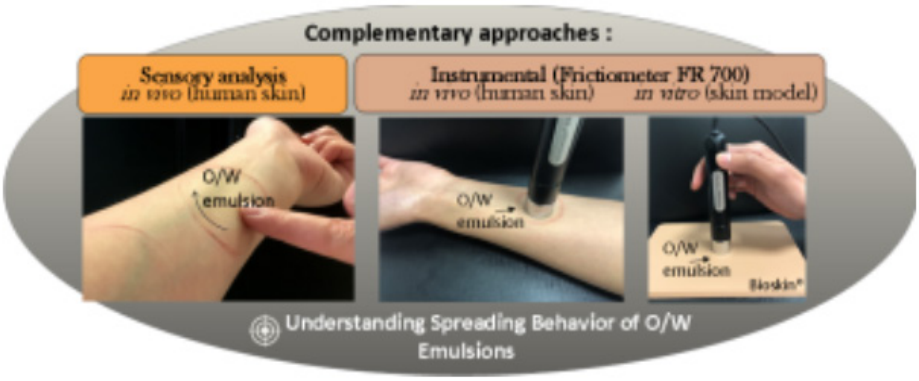
Today's consumers are looking for environmentally friendly cosmetic products without making any concessions on their performance [1] including sensory qualities and efficiency. In such a competitive sector as cosmetics, the development of innovative tools to gain time and to better understand the product application and the skin-product interaction is therefore crucial [2–3]. Here, the aim is to present a tactile sensory evaluation approach for skincare products and to introduce a case study of how combining different approaches such as sensory analysis, physico-chemical methods and biometrology are of key interest to whom aim to understand the complex mechanisms for tactile perception induced by product application on the skin surface.



A series of either basic and original methods using human skin as well as non-biological surfaces mimicking the human skin were successfully tested with very good reproducibility of the spreading behavior. The study allowed deepening both knowledge and understanding of skin interactions with its environment, after application of dermocosmetic emulsions. In addition, results clearly highlight how emulsion composition do influence the penetration and absorption in the human skin, thus bringing keys for better understanding the spreading behavior. Finally, the developed original tools are of great interest to study the efficacy of new formulas on skin and help performing standardized measurements as well as solving the logistic and safety problems of in vivo studies. Undoubtedly, in vivo tactile sensory evaluation is an essential tool for cosmetic products characterization. In a fast-growing society the development of innovative instrumental and fast alternative methods highly correlated to in vivo studies represents a promising way to control the sensory perception of new products which is very important for their acceptability by consumers.

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Keywords: Sensory evaluation, human skin, skin models, alternative tests

UNDERSTANDING THE EVAPORATION OF THE FRAGRANCES FROM THE SKIN

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The balance between absorption and evaporation occurs when a topical product is applied onto the skin surface. It is a complex phenomenon that depends on the ingredients contained in the product. Among ingredients, odorous compounds have a key issue since their release is linked to the smell of perfumes. It has been shown that contact with skin slows down the evaporation of odorous compounds compared to inert ceramic support [1], which proves that interactions with the stratum corneum take place. Depending on the nature, polarity and affinity of the fragrance compounds forming the residual film, they are more or less able to interact with the skin. Nevertheless, other properties such as roughness, hydration or the presence of sebum at the skin surface also play an important role in the release phenomena. However, to our knowledge, these aspects have been little or not developed in the literature and need to be studied in depth for a better understanding of the connection between surface physicochemistry and evaporation phenomena. To answer this problem, the mechanisms of absorption and evaporation occurring on the surface of the skin after application of a fragranced formulation must be studied and understood. The first step consists to study exhaustively these two phenomena by considering the influence of the composition and the physicochemical characteristics of the applied product, the properties of the skin and, finally, the lipidic composition of the surface. Experiments were carried out with a double approach combining in-vivo and in-vitro measurements. The evaporation of a thoughtfully chosen mixture of fragrances was analyzed using headspace-gas chromatography after application onto the skin or model surfaces. Our results made it possible to better understand the impact of skin properties both on fragrance release in the air and on retention into the residual film at the cutaneous surface. The effects of time and the chemical composition of the fragrance were also studied to propose a comprehensive review of phenomena occurring at the skin surface after applying a fragranced formulation.

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X-RAY DIFFRACTION – A SENSITIVE TOOL FOR ASSESSING COLLAGEN QUALITY IN COSMETIC TESTS

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The structure of the collagen is a good marker to assess the effectiveness of anti-aging or emollient products in dermis. Histological observation of ex vivo skin explants by optical microscopy is limited to the cellular scale. To go beyond, other microscopies like AFM and biphoton provide information at higher resolution. However, the areas that can be reasonably analysed are micrometric and therefore may not be representative of the whole skin sample. Moreover, these techniques are not always well adapted to routine analysis of series of explants required for efficacy tests. To overcome these limitations, we propose to use Small-Angle X-ray Scattering (SAXS), a technique highlighting the quality of the collagen with high precision and sensitivity, averaged over millimetric areas. Like all X-ray scattering techniques, SAXS is sensitive to the molecular packings. The more they are periodic, the more diffracted X-rays concentrate in well-defined directions in space. In collagen, the triple helices are arranged extremely evenly along the microfibrils, which leads to the well-known 65 nm striated structure and to very sharp and intense peaks in SAXS. The positions and intensities of the series of peaks are indeed a very sensitive marker of the internal organization/quality of collagen microfibrils. This organization may depend on physiological factors (origin, age, mutation, pathology) as well as physical/chemical factors (moisture, treatment). Very small and/or early changes not detectable by microscopy techniques can be detected by SAXS. In practical terms, SAXS measurements can be performed on sections of cryopreserved skin explants that have previously been treated under survival conditions. The best data are obtained with synchrotron X-ray sources, but a conventional source can also be used with slightly thicker samples. Dozens of samples can be analysed rather quickly (less than 3h), and the data analysis is rather simple and possibly semi-quantitative. Thus, the technique is well suited for tests evaluating the effectiveness of treatments. The use of the SAXS technique to characterize the collagen of ex vivo skin explants should not replace microscopy techniques but should be considered as a complement to evaluate the internal quality of microfibrils and to detect early structural modifications.

DUPONTTM LIVEOTM SILICONE TOPICAL EXCIPIENTS ADDRESSING DRUG DELIVERY PERFORMANCE CHALLENGES FOR SKIN DISORDERS MANAGEMENT

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Topical applications are designed to treat various skin conditions and mainly marketed as prescription or consumer healthcare products. Prescription market requirements include safe and effective delivery of the API (active pharmaceutical ingredient) to efficiently achieve pharmacokinetic and clinical relevance. In contrast, the consumer healthcare market strongly favors the sensory aspects of a formulation; this includes efficacy with a pleasant feel to help patients be more compliant with their treatment. DuPontTM LiveoTM silicones are widely used in various medical applications and dermatological therapies from transdermal to topical applications. Formulations with silicone material offer various dosage forms and textures for dermatological formulations such as spray, gels, lotions, patches and creams that deliver active pharmaceutical ingredients effectively. Furthermore, silicone enhances other formulation benefits such as proven aesthetics, functional film characteristics and long-lasting effect well adapted for different skin diseases. In our seminar, we will go through recent studies where silicone technologies have been successfully used as topical excipients in different dermatological formulation concepts. Formulation concepts presented are developed with innovative silicone excipients to help tackle today's healthcare challenges, provide drug delivery efficacy and encourage patient compliance.

Formulation concept:

• Concept 1- Spray for ostomy - is based on the development of a formulation containing silicone resin blend that forms an invisible and conformable film on the skin.

• Concept 2 – Gel for scar – is based on the long history of silicone gel efficacy in scar management by providing pleasant feel and long lasting on skin.

• Concept 3 – cream for psoriasis - the aim of this development is for a cream loaded with betamethasone dipropionate and designed to treat psoriasis and improve patient compliance

• Concept 4 – emulsion for acne - The aim of this concept is to develop a cream that delivers salicylic acid combined with the non-comedogenic properties of silicone.

These studies also emphasize the versatility of silicone chemistry that provides a wide range of technologies with various functionalities to formulators to develop formulations for diverse pharmaceutical applications. Silicone technologies are used as topical excipients in dermatological formulations to improve sensory benefits and efficient delivery of drugs.

DUPONTTM LIVEOTM TOOLBOX OF INNOVATIVE SILICONE RESIN BLENDS AND FILM FORMING FORMULATIONS FOR TOPICAL INDICATIONS

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Silicones are widely used in various medical and pharmaceutical applications such as wound and scar management devices, topical and transdermal therapeutic systems. Silicones have been successfully formulated as pharmaceutical excipients in dermatological and topical drug delivery forms to improve their efficacy and acceptance by the patients. Film formers are polymers capable of forming a cohesive and continuous film after evaporation of the volatile solvent on the skin with optimal adhesion and flexibility properties. Film-forming formulations are used in topical applications to provide substantivity, comfort and long-lasting properties. While the use of film formers in the field of wound care is already established and well accepted by patients, film-forming systems are still an exception in the treatment of skin diseases. Nevertheless, we are observing increased interest from the scientific community and healthcare industry for applications where film formers are used as novel delivery forms This presentation will focus on key film attributes associated to DuPontTM LiveoTM technology portfolio of Resin Blend technologies. This study opens various future prospective for the use of silicone excipients as film formers that would enable formulating topical dosage forms combined with specific film properties such as long-lasting substantivity, and wash off resistance. Thus, offering the formulators and/or end users a product that would help achieve patient compliance, safety and efficacy.

NANOPARTICULATE SYSTEMS FOR DERMAL DELIVERY OF ANTIMYCOTICS

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Fungal infections are among the most common diseases worldwidely and almost more than a billion people are reported due to having skin, nail and hair mycosis with high incidence.1 Although many preparations are commercially available for topical treatment, most of antimycotics are poorly soluble in water and large molecule. These troublesome properties lead to low permeability and poor bioavailability into the skin. Nanoparticulate formulations are great candidates to overcome such troubles in dermal delivery of drugs. Within the scope of this study, we aim to develop specifically tailored polymeric and lipid-based nanoparticles and evaluate their potential use for topical delivery of two antimycotics, namely itraconazole (ITZ) and ketoconazole (KTZ), to overcome their insufficient physico-chemical natures in order to increase their bioavailability into the skin. ITZ and KTZ loaded PLGA nanoparticles, ITZ loaded nanoemulsions (NEs) and KTZ loaded lipid nanocapsules (LNCs) were synthesized and characterized in terms of their physicochemical properties such as particle size, shape, particle homogeneity, surface charge, drug loading capacity, encapsulation efficiency, short and long-term stability. Finally, we are able to reach stable nanoformulations with particle size of around 200-300 nm and low polydispersity containing 0.2% ITZ (PLGA and NEs) and 0.75% with KTZ (LNCs). A freeze-drying step was added to long-term stabilize the systems. The best systems were determined by ex vivo permeation study on porcine skin in Franz diffusion cells. The efficiency of the developed nanoparticulate systems to deliver ITZ or KTZ into the skin tissue was successfully confirmed.

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OPTIMIZATION OF PROTEIN LOADED PVP/VA DISSOLVABLE MICRONEEDLE ARRAY BY USING DESIGN OF EXPERIMENT (DOE) APPROACH

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In recent years, the Design of Experiment (DOE) approach gained huge attention in academic research and the pharmaceutical industry alike. (1) It allows an investigation of multiple factors at a time rather than following a trial-and-error strategy to optimize a process or product. Even though protein drugs became first line therapeutics for various diseases in the last years (2), most of them still required parenteral administration which comes with many disadvantages including associated discomfort, biohazardous waste and risk of infection. Dissolvable microneedle (DMN) arrays are a pain free alternative that allows for non-invasive self-administration of protein drugs. (3) However, biomolecules are prone to aggregation, degradation, and conformational changes in a non-physiological environment. (4) Hence, a thorough formulation design is essential to maximize drug stability and microneedle performance as well as minimize immunogenicity. This study focuses on the application of DOE to optimize PVP/VA dissolvable microneedle arrays as protein delivery systems. PVP/VA dissolvable microneedles were fabricated using the micromolding technique and bovine serum albumin (BSA) as a model protein. The microneedle formulation was optimized using mixture design approach coupled with statistical applications. The effects of the amounts of stabilizing excipients such as phosphate buffer salts and sugar components, on microneedle appearance and protein stability were analyzed. BSA-loaded dissolvable microneedle arrays were characterized immediately after fabrication using Light Microscopy, High Performance Liquid Chromatography (HPLC) and Circular Dichroism (CD). Furthermore, DMN mechanical strength measurements and a short-term stability study at room temperature were conducted to complement data for DOE. BSA-loaded PVP/VA microneedles were successfully fabricated. We verified the process of optimizing a microneedle formulation using the mixture design approach in association with various statistical estimations. The influence of the investigated factors on the DMN appearance and the protein stability was demonstrated. The study also revealed the influence of phosphate buffer salts on BSA loading efficiency. The optimized DMN formulation showed its good properties in terms of the mechanical strength when stored at room temperature. This study demonstrates how key formulation and design parameters can be optimized to improve stability and loading efficiency of a protein-containing dissolvable microneedle array.

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PCL PATCHES WITH ANTIMICROBIAL SURFACES FOR WOUND HEALING APPLICATIONS

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Skin is the largest organ of the body that performs several functions such as barrier function, protection from microbes, thermoregulation etc. Being the outermost layer of the body, it is in continuous contact with the outer environment and is highly prone to damages such as wounds. Moreover, the attachment and proliferation of bacteria to various surfaces leads to the formation of biofilms, which induce complications in humans. Wound healing has progressed a lot in the past decade from conventional treatments such as ointments and gauze coverages to the implementation of advanced multi- functional wound dressings. A physical antibacterial method includes the incorporation of nanosized structures which damage the cell wall of the bacteria when they attach to the surface, thus effectively killing them [1]. Currently, biocompatible are categorized into natural and synthetic biocompatible polymers. Synthetic polymers include polycaprolactone (PCL), polylactic acid (PLA) and polyglycolic acid (PLGA) which are inexpensive and easy to manufacture [2]. Herein, a series of PCL polyesters with various molecular weights were successfully synthesized using the well-known ring opening polymerization (ROP). In a further step, three-dimensional (3D) nanosized columns were fabricated using a Polydimethylsiloxane (PDMS) mould. The structure and crystallinity of the PCL samples was evaluated using Fourier transform infrared spectroscopy (FT-IR) and X-ray Powder Diffraction (XRD). Finally, the obtained nanostructures were optically observed using Scanning Electron Microscopy (SEM), while the cell adhesion and their antimicrobial properties were also investigated.

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Use a numbered list of references at the end of the article. See the example of citation below. Your references should be published materials accessible to the public.

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SYNTHESIS AND CHARACTERIZATION OF HEMOSTATIC PATCH BASED ON CHITOSAN WITH ENHANCED ANTIBACTERIAL ACTIVITY.

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Hemostasis is the first stage of the wound healing process activated upon injury, that results in the control of bleeding and the formation of a protective barrier [1]. The mechanism of hemostasis includes: 1) vasoconstriction, 2) formation of a platelet plug, and 3) blood coagulation [2]. During the hemostasis process, wound infection can exist, inhibiting epidermal maturation and may cause bacteraemia, sepsis, and multiple-organ dysfunction syndrome. In cases of severe wounds, the use of hemostatic products with antimicrobial properties is necessary to compensate for the compromised first step of wound closure [3]. According to the United States' military statistics, nearly 50% of deaths on the battlefield are caused by excessive bleeding, whereas more than 15% of the casualties are completely preventable. Chitosan (CS) is as a naturally derived polymer that plays a leading role in the development of new hemostatic products [4]. CS is a cationic polysaccharide with bactericidal properties, renewable, nontoxic, biodegradable and hydrophilic with high reactivity, promotes coagulation, flocculation and biosorption. The hemostatic properties of chitosan are due to direct electrostatic interactions between negatively charged red blood cells and platelets and the positively charged CS. Researchers and pharmaceutical companies are focusing on the hemostatic properties of CS by formulating it into several hemostatic products. Ongoing research is focusing on advanced hemostatic CS-based materials with enhanced antimicrobial properties, good biocompatibility, rapid hemostatic ability, and low manufacturing cost. Hence, in this work, a grafted chitosan copolymer with [2-(N-morpholino) ethanesulfonic acid (MES)] was been synthesized by free-radical polymerization. CS-g-MES porous sponges were prepared using a modified thermal-induced phase separation process fabricating a porous patch which was confirmed by various characterizations. For example, the successful synthesis of the material was confirmed by FT-IR, its crystallinity was researched by XRD, the porous morphology of the patch was analyzed with SEM images, and water swelling was also investigated.

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SYNTHESIS AND CHARACTERIZATION OF POLY (BUTYLENE SUCCINATE) NANOPARTICLES LOADED WITH HEPARIN FOR HEMOSTATIC APPLICATIONS

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Bleeding complications usually cause significant morbidities and mortalities in injured cases of civilian or military. Effective hemostasis has paramount clinical significance in prophylactic, surgical, and emergency. [1] Irregular wound bleeding or uncontrollable massive bleeding is the primary cause of traumatic death in wars or accidents.[2] The death caused by massive blood loss from penetrating injuries accounts for about 50% of the total death in wars. Therefore, the excellent hemostatic performance of hemostasis is of great significance for saving lives. Recently different hemostatic agents have been developed, but most of them are ineffective in stopping severe bleeding and are expensive or cause safety concerns such as further thrombosis in unwanted places [3]. It has been clinically reported that several hemostatic products were detected in various parts of the human body (e.g. lungs) after their use, leading to blood clots and finally causing various problems up to death. So, in recent years hemostatics with a low concentration of anticoagulants (eg heparin) have been developed to avoid further thrombosis. However, the activity of hemostatic products with antithrombotic additives may affect the hemostatic properties of the products. Thus, there is great interest in the development of novel effective hemostats to achieve hemostasis, avoiding further side effects. In the present work, active substance heparin was encapsulated in poly(butylene) succinate (PBSu) nanoparticles, in order to be released as an antithrombotic drug of the blood vessels after the action of the hemostatic patches. PBSu porous nanoparticles were prepared using dichloromethane (DCM) as a solvent and polyvinyl alcohol (PVA) as a surfactant. The composition of the nanoparticles, their size, and their morphology were studied by Dynamic Light Scattering (DLS) and Scanning electron microscope (SEM) techniques. The size of the empty nanoparticles was 500 nm while the nanoparticles loaded with heparin presented a size of about 800 nm. The structure of the nanoparticles before and after encapsulation was well-formed with spherical size. The successful synthesis of the produced nanoparticles was confirmed by Fourier-transform Infrared (FTIR) and their thermal stability using the DSC method.

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THERAPEUTIC STRATEGIES FOR THE MANAGEMENT OF HAIR LOSS: THE ROLE OF PHARMACEUTICAL TECHNOLOGY

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Hair loss is a common autoimmunity disorder due to multiple reasons, such as aging, diseases, and stress. About 50% of men and 15–30% of women suffer from hair loss and it is often a source of considerable psychological and social distress. Nowadays, there are many approved treatments and pharmacological therapy, especially through topical administration, is the main therapeutic strategy to stimulate hair regrowth [1]. Current strategies focus primarily on stimulation of existing follicles, but often the skin barrier prevents drugs from selectively reaching the target follicles, necessitating high concentrations or several applications a day [2]. This could lead to the appearance of side effects, such as inflammation, redness, itching, oily hair, resulting in low patient compliance. Therefore, an interesting approach to obtain increased drug effectiveness could be the use of drug delivery systems, capable of convey biologically active molecules and favoring their controlled release, increasing their stability and facilitate their targeting at the skin level [3]. The aim of the study was to prepare and characterize a nanosystem suitable for topical administration, whose constituents could enhance the action of the delivered drug. A deep physical-chemical characterization was carried out evaluating size, PDI, ζ-potential, fluidity, microviscosity, polarity. To evaluate the loading and release capability of the formulated nanosystem, in vitro release studies were performed using either a dialysis membrane, consisting of regenerated cellulose (MWCO 8000) or a vertical Franz cell, employing an artificial membrane, Strat-M. The formulated nanosystem has been tested in vivo, on patients divided into 5 groups (volunteers and aged between 18 and 60). Initially the tolerability of the nanosystem in topical treatment was evaluated and subsequently the efficacy of the treatment was monitored by global photography, photofinder dermoscope and trichoscan professional. Finally, to confirm the local action of the treatment, studies were conducted by analyzing the serum of treated patients to quantify traces of drugs or their metabolites.

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TRANSDERMAL HUMAN SKIN PERMEATION STUDY OF A NANOPARTICLE CONTAINING A DERIVATE FLAVANONE FROM NATURAL RESOURCES

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Flavanones are part of a family of naturally occurring polyphenolic compounds. They possess a wide range of biological activities such as antimicrobial, antifungal, antioxidant, neuroprotective and anticancer activities [1]. Furthermore, the poor solubility of flavanones that restrict its bioavailability, due their chemical structure, can be overcome using a nanoscale drug delivery system [2]. We investigated the transdermal human skin permeation of the derivative flavanone (2S)-5-hidroxi-7-metoxi-6-(3-metil-2-buten-1-il)-2-fenil-2,3-dihidro-4H-1-benzopiran-4-ona (1') carried in a Polylactic-co-glycolic acid (PLGA) nanoparticle obtained from the derivatization process by acetylation reaction from natural flavanone (2S)-5,7- dihydroxy-6-(3-methyl-2-buten-1-yl)-2-phenyl-2,3-dihydro-4H-1-Benzopyran-4-one (1) extracted from Eysenhardtia platycarpa [3]. Moreover, we prepared polymeric nanoparticles flavanone 1' (NP1') by solvent displacement technique with PLGA and P188. We determined the particle size and performed the ex vivo permeation studies with vertical Franz diffusion cells using dermatomed human skin as membrane (n = 3). Samples were removed at different time points for 24 h. Validated HPLC method was used to quantify the flavanone. We done the flavanone skin extraction by sonication with a mixture of Ethanol: water (70:30). The results obtained showed a NP1' Z-average of size of 178.03 ± 1.33 nm; 78.8 µg of permeated flavanone and 1.4 g/g skin/cm2 of retained flavanone amount after 24 h in the skin and, 408.9 µg/h of average flux.

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CURCUMIN NANOMICELLES FOR THE TOPICAL TREATMENT OF MELANOMA

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The study aimed at developing curcumin-loaded nanomicelles for skin application to target melanoma cells, avoiding systemic adverse events. Curcumin is known for its several pharmacological properties including anti-inflammatory, antimicrobial, anticancer and antioxidant activities [1]. However, it presents some disadvantages related to the scarce stability of the molecule for the presence of reactive groups in the molecular structure and to the fact that it is highly insoluble in aqueous medium [2]. To overcome these limitations, nanomicellar formulations based on binary mixture of surfactants to solubilize curcumin in a hydrophilic environment and to extend its stability from autoxidation and photodegradation reactions have been tuned up. The choice of surfactants was based on their ability to create stable, safe and biocompatible nanomicelles. Different types of surfactants were tested, finally selecting Vitamin E-TPGS and Kolliphor ELP. Vitamin E TPGS is approved as adjuvant in drug delivery systems by FDA and widely reported in literature for topical use. Similarly, Kolliphor ELP has been used safely in dermatological formulations at concentrations up to 4% w/w [3, 4]. The formulations were characterized in terms of pH, size by dynamic light scattering, amount of curcumin solubilized and encapsulation efficiency by HPLC. Furthermore, a suitable Design of Experiment (DOE) study to evaluate the effect of two surfactant's ratios in drug loading, size and wettability and to select the best performing formulation have been settled for optimization of the development phase. Then, the nanomicelles were analysed by Fourier-transform infrared spectroscopy (FTIR) to evaluate the interaction of curcumin with the surfactants and assess the encapsulation of curcumin inside the lipophilic core of nanomicelles. Stability studies of the selected formulation were carried out in different conditions in terms of light exposure and temperature to investigate both the stability of the formulation itself and of the encapsulated curcumin. Besides, to reach the goal of developing a nanomicellar system that could efficiently deliver curcumin to the skin, in vitro release studies and in vitro cutaneous permeation studies were performed both at physiological pH and acidic pH to simulate tumoral environment. Finally, the cytotoxicity of curcumin-containing nanomicelles was evaluated on melanoma cell lines to investigate the activity of the formulation against skin cancer.

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DERMAL DELIVERY OF PHYTOCHEMICALS: STORAGE STABILITY OF MONO- AND MULTIPHASE SYSTEMS WITH PANAX GINSENG EXTRACT AND SKIN PERMEATION EX VIVO

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Plant extracts with antioxidative, anti-inflammatory and wound-healing activity are valuable dermopharmaceutical assets in times of increasing antibiotic resistance and failure of trade chains. However, formulation strategies for such multicompound agents are scarce. Their effect on technological properties of vehicles and the active compounds potential to actually cross the stratum corneum barrier is often unknown. Therefore, panax ginseng root extract was investigated as antioxidative plant extract with ethnomedicinal use. Mono- and multiphase vehicles (o/w nanoemulsions and hydroalcoholic polymer-based gels) were developed and characterized by dynamic light scattering, pH, rheological assessment and monitoring of ginsenoside Rg1 and Rb1 content through UHPLC/MS over 12 weeks. Skin permeation was evaluated ex vivo (diffusion cells, porcine ear skin) for ginsenosides Rg1 and Rb1 via UHPLC/MS. Results showed superior storage stability and skin permeation of carbopol-based hydrogels with 20% w/w ethanol, and confirmed skin permeation of Rg1, but not Rb1 under the given experimental conditions. Current studies are investigating the effect of pH adjustment to improve storage stability. In addition, in vitro cytotoxicity studies and scratch assays using human dermal primary cells will serve to evaluate biocompatibility of the developed vehicles and their biological effects.

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EVALUATION OF THE TRANSDERMAL ABSORPTION OF OLIVE OIL-BASED FORMULATIONS LOADED WITH BARICITINIB FOR THE TREATMENT OF ALOPECIA AREATA

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Alopecia areata is an autoimmune disease that causes hair loss because hair follicles are attacked by the immune system. Baricitinib (BCT) (2-(3-(4-(7H-pyrrolo[2,3-d] pyrimidin-4-yl)-1H-pyrazol-1-yl)-1-(ethylsulfonyl) zetidine-3-yl) acetonitrile), with a molecular weight of 371.42 g/mol (C16H17N7O2S) is a small molecule able to modulate the signaling pathway of JAK like an inhibitor [1]. BCT is considered an immunosuppressant drug that is a Janus kinases 1 and 2 selective inhibitor (JAK). The proposed solution for skin is Olive oil loaded with BCT. Olive oil has been used for centuries to treat different pathologies, some of them recognized in the European pharmacopoeia: inflammation, hypertension and gout are a few examples [2]. Olive oil, containing oleic acid and smaller amounts of linoleic acid and palmitic acid, is useful for hair offering softness and moisture. Even more, olive oil's moisturizing properties may also help strengthen the hair and increase its elasticity, helping to prevent breakage or split ends. Therefore, the main purpose of this work was to study the effectiveness of formulation in combination with BCT and transcutol® P to stimulate hair growth as part of alopecia treatment. The detailed Oil formulation characterization, ex vivo permeation studies through skin tissues and, the antioxidant properties were evaluated. For this purpose, Olive oil with Baricitinib was prepared with 2ml of Transcutol. The permeation tests were conducted on Franz cells under sink conditions using a biocompatible receptor fluid and human skin dermatomed at 0.4 mm. The system was thermostated at 32oC and 300µL of the formulation was applied to the skin. Samples were collected within 24h, which were stored at -20oC until they were analysed by a validated HPLC method. Antioxidant test is a popular, quick, and easy routinely accomplished for measurement of antioxidant molecules properties using free radicals for assessing its potential to serve as hydrogen providers or free-radical scavengers (FRS). All samples in this work assayed against stable DPPH were determined spectrophotometrically with a slightly modified test Brand-Williams. The results show that Olive oil was able to increase the permeation across the skin (flux: 0.062 ± 0.001µg/h). It could be said that the antioxidant values of BCT ethanolic solution not reflected an antioxidant property and also the BCT presence in the Olive oil-BCT potentiated the antioxidant activity of Olive oil.

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FORMULATION OF A 2-IN-1 SHAMPOO BASED ON COCOS NUCIFERA OIL (ARECAEAE) FOR THE PREVENTION OF TRACTION ALOPECIA IN BLACK WOMEN

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Traction alopecia is very common in black women. It causes inflammation of the scalp, which in severe cases can become irreversible. Cocos nucifera oil is highly prized for its soothing, regenerating and protective properties for the hair fiber. The aim of our work is to formulate a 2-in-1 shampoo based on this oil for the prevention of traction alopecia in black women. After harvesting, identification and characterization of the raw materials, the oil was cold extracted. The oil obtained was characterized. Several shampoo formulas were proposed and tested. The selected formula was characterized from a physicochemical and rheological standpoint. Its foaming power was determined using the Ross-Miles method. A 28-day stability study was carried out. The oil was clear, pale yellow in color, with a faint odor. Its HLB was 8. Its various physicochemical parameters were: refractive index 1, 4485 - 1.4495, peroxide 0.27, saponification 255 - 258, iodine 8 - 9.5. The shampoo selected had a pH of 6.10 at 10% and 5.04 at 26.2°C. It was O/W type, stable under various conditions, with good foaming power. Its viscosity was 0.00152133 m2.s-1 at 27.4°C. The shampoo obtained showed good physicochemical and rheological properties for use in hair care. This study merits further investigation.

Key words: Shampoo, Cocos nucifera, alopecia, Black woman

ANTI-STRETCH MARKS COSMETICS: ACTIVES AND FORMULATIONS AMONG MARKETED PRODUCTS

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Stretch marks are described as cutaneous lesions that develop as a result of the dermis extending. Although they are considered the most frequent benign skin lesions, they may affect self-esteem and even result in mental distress.[1-3] While some individuals experience no symptoms, others may feel irritation, burning, or discomfort in their bodies.[3] There are some topical agents (drug products and cosmetics) used to prevent/improve the appearance of the lesions, as well as other more or less invasive options (laser radiofrequency, phototherapy, platelet-rich plasma, microdermabrasion, and microneedling approaches). [4-5]This market study was designed to identify anti-stretch marks products marketed in pharmacies, parapharmacies and supermarkets in Portugal and analyze their active ingredients, formulation and claims. A total of 35 cosmetic products from 22 different brands were collected. Most products (74%) were developed for pregnant and/or pubertal women and were presented as leave-on oils (43%) and creams (34%). Only 3 products were designed as multifunctional (use for other marks and scars besides striae) and only 43% mentioned the adequate frequency of application (mostly twice a day). Active ingredients were mainly from plant origin (in 91% of the products) which is explained by the direct impact on regeneration, and collagen fibers of vegetable oils and butters (sunflower, hiprose, almond) and different extracts from plants (mainly Centella asiatica and Equisetum arvense extracts). Combination of active ingredients was found in 22 products showing the importance of additive/synergic effect for efficacy. Claim substantiation through clinical trials was identified for 20 different cosmetics (57%). Among these, 10 do not specify the population of the study, while 8 were tested among pregnant women. Products marketed in pharmacy were found to combine more active ingredients and present more clinical studies that those found in supermarkets. These results will be used as benchmark to support the development of new anti-stretch marks cosmetic products.

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ARTEMETHER AND LUMEFANTRINE DISSOLVING MICRONEEDLE PATCHES WITH IMPROVED PHARMACOKINETIC AND EFFICACY FOR UNCOMPLICATED MALARIA CAUSED BY PLASMODIUM FALCIPARUM

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Malaria affects more than 200 million people annually around the world, killing a child every 2 min. Artemether (ART) and lumefantrine (LUM) are the gold standard choice to treat uncomplicated Plasmodium falciparum malaria; however, they are hydrophobic compounds with low oral bioavailability. Microneedle (MN) arrays consist of micron-sized needles on one side of a supporting base and have the ability to bypass the skin's stratum corneum barrier in a minimally invasive way, creating temporary channels through which drugs can diffuse, including those with poor water solubility. Herein, we report the development of dissolving MNs (DMNs) containing ART (MN-ART) and LUM (MN-LUM) as an alternative treatment regimen for malaria in low-resource settings. To incorporate the drugs into the MNs, nanosuspensions (NSs) for both molecules were developed separately to enhance drug solubility. The NSs were freeze-dried and the powder form was incorporated directly in an aqueous polymeric blend with poly-vinyl-pyrrolidone for MN-ART and a sodium hyaluronate hydrogel for MN-LUM. The in vivo bioavailability studies were performed using an MN reapplication scheme (1 × a day for 3 days), illustrating that an extended-release profile was achieved for both drugs when MNs were applied intradermally, and when compared to conventional oral treatment. The ART-LUM oral treatment was used as a positive control. For antimalarial activity, studies with animals infected with 106Plasmodium yoelii 17XNL (12 days) were also conducted using female C57BL/6JUnib mice, demonstrating a 99.5% reduction in parasitemia by day 12 post-infection. By abolishing the infection, MN-ART and MN-LUM may serve as promising controlled intradermal delivery devices for antimalarial drugs to be explored in endemic areas.

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