Skin Forum 2025
Annual Meeting

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Berlin, Germany

Abstract book

APV MAKING SCIENCE WORK

Skin Forum
international skin science network

A conference organised by The International Association for Pharmaceutical Technology and Industrial Pharmacy in partnership with Skin Forum

Abstracts of poster presentations

Posters will be continuously exhibited on Tuesday from 08:45 - 18:00 h, with special sessions with authors presenting from 10:35 - 11:05 h, 12:25 - 14:10 h and from 16:45 - 18:00 h. As well as on Wednesday from 08:45 - 17:00 h, with special sessions with authors presenting from 10:20 - 10:45 h, 12:25 - 13:30 h and from 14:40 - 15:10 h.

P01. Exploring the potential of plant hydrolates in green cosmetic formulations: case study of Pannonian thyme hydrolate

Milica Lukić M[a], Vanja Todorović[b], Zoran Maksimović[c], Dragana Božić[4]
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b Faculty of Pharmacy – University of Belgrade, Serbia, Department of Bromatology
c Faculty of Pharmacy – University of Belgrade, Serbia, Department of Pharmacognosy
d Faculty of Pharmacy – University of Belgrade, Serbia, Department of Microbiology and Immunology

P02. Evaluation of natural waterless face cleansers: physicochemical properties and performance assessment

Ana Ćirić[a], Ljiljana Djekic[a], Milica Lukić[a]
a Department of Pharmaceutical Technology and Cosmetology, University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia

P03. Application of PBPK modelling to optimise IVPT study design and predict the impact of formulation changes on skin permeation

Y. Zhang[a], N. Murthy[b], D. Paterson[a], S. Polak[a],d, Y. Dancik[a], E. Tsakalozou[c], P. Ghosh[c], J. Clarke[a]
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b Topical Products Testing LLC, Mississippi, USA;
c Office of Research and Standards (ORS), Office of Generic Drugs (OGD), Center for Drug Evaluation and Research (CDER), US Food and Drug Administration (FDA), Silver Spring, Maryland, USA;
d Jagiellonian University Medical College, Faculty of Pharmacy, Poland

P04. A Pivotal, Dermal, In-Vivo Bioequivalence Study performed by Confocal Raman Spectroscopy (CRS)

J. Link, C. Heusel and D. Lunter
Department of Pharmaceutical Technology and Biopharmacy, University of Tuebingen, Tuebingen, Germany

P05. Topical delivery of terbinafine: In-vivo studies

ASM Monjur Al Hossain[1a, b], Bruno Sil Dos Santos[2c], Jonathan Hadgraft[3a], Majella E. Lane[4a]
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b Dept. of Pharmaceutical Technology, University of Dhaka, Dhaka-1000, Bangladesh
c Department of Pharmaceutical Science and Pharmacology, London Metropolitan University, 166-220 Holloway Road, London, N7 8DB, United Kingdom

P06. Bioadhesive chitosan films loading curcumin for safe and effective skin cancer topical treatment

Seila Tolentino[a], Mylene M. Monteiro[b], Felipe Saldanha-Araujo, Marcilio Cunha-Filho[a], Tais Gratieri[a], Eliete N. Silva Guerra[b] and Guilherme M. Gelfuso[a]
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b Laboratory of Oral Histopathology, University of Brasilia, Brasília, Brazil
c Laboratory of Hematology and Stem Cells, University of Brasília, Brasília, Brazil

P07. Influence of nanoparticles'characteristics on iontophoretic targeted deposition to the hair follicles

Jayanaraian F Martins[a], Agnes-Valencia Weiss[b], Marcilio Cunha-Filho[a], Guilherme M. Gelfuso[a], Marc Schneider and Tais Gratieri[a],
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b Department of Pharmacy, Biopharmaceutics and Pharmaceutical Technology, Saarland University, Saarbrücken, Germany

P08. Characterization of Cimetidine for Topical Delivery

Lu Han[a], Bruno Da Silva Sil Dos Santos[b], Majella Lane[a]
a School of Pharmacy, University College London, London, UK
b London Metropolitan University, London, UK

P09. Dermal delivery of phytochemicals: Release of ginsenosides from topical formulations with Korean red ginseng extract ex vivo

Tanja Pfleger[a], Karin Ortmayr[b], Katja Steiner[a], Rawan Zaher[a], Saskia Seiser[c], Adelheid Elbe-Bürger[c], Elke Heiss[b], Victoria Klang[a]
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b Department of Pharmaceutical Sciences, Division of Pharmacognosy, University of Vienna, Vienna, Austria
c Department of Dermatology, Medical University of Vienna, Vienna, Austria

P10. Understanding Skin Barrier Formation: Insights from Lipid Model Systems
Andrej Kováčik[a], Iva Hrdinová[a], Petra Pullmannová[a], Tomáš Havrišák[a], Lukáš Opálka[a], Jaroslav Maixner[b], Kateřina Vávrová[a]
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b Faculty of Chemical Technology, University of Chemistry and Technology in Prague, Prague, Czech Republic

P11. New aspects about the impact of ceramides to the substructure of the Stratum corneum barrier function
Adina Eichner[a,b], Lukáš Opálka[c], Thomas Haußd , Gerald Brezesinski[b]
a Department of Dermatology and Venereology, Martin Luther University Halle-Wittenberg, Halle (Saale), Germany
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c Skin Barrier Research Group, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic
d Joint Research Group Macromolecular Crystallography, Helmholtz Institute Berlin, Berlin, Germany

P12. Bioequivalence assessment of topical products in focus: A feasibility study and the new EMA Guideline
Adina Eichner[a,b], Yahya Mrestani[a,b], Martin Hukauf[c], Johannes Wohlrab[a,b]
a Department of Dermatology and Venereology, Martin Luther University Halle-Wittenberg, Halle (Saale), Germany
b Institute of Applied Dermatopharmacy at Martin Luther University Halle-Wittenberg (IADP) e.V., Halle (Saale), Germany
c StatConsult GmbH, Magdeburg, Germany

P13. A clinical dermal open flow microperfusion (dOFM) study to assess bioequivalence (BE) of different topically applied diclofenac products
Katrin Tiffner[a], Tannaz Ramezanli[b], Thomas Birngruber[a], Manfred Bodenlenz[a], Reingard Raml[a], Sonja Kainz[a], Sam G. Raney[b], Frank Sinner[a]
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b Office of Research and Standards, Office of Generic Drugs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, Maryland, USA

P14. Assessment of Skin Permeation using Stimulated Raman Scattering Imaging and In-Silico Modelling Anukrati Goel[a], Natalie Belsey[a,b], Tao Chen[a]
a School of Chemistry and Chemical Engineering, University of Surrey, Guildford, UK
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P15. Innovate in topical: sprayable vehicles for patient-friendly
GAVINET B.[a], GOUTTE-QUILLET M.[a], ROSO A.[a]
a Research & Innovation, Seppic, Castres, France

P16. Cerosomes for Advanced Therapy of Inflammatory Skin Diseases
Nikola Strnádková[1], Jarmila Zbytovská[1]
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P17. Shelf life of fresh and frozen skin for in vitro dermal absorption, skin permeation and skin penetration tests
K. Damrau[1], D. da Silva[2], A. Sattler[1], R. Lagoa[2], A. Ullrich[1]
1 PRIMACYT Cell Culture Technology GmbH, Germany
2 LSRE-LCM, School of Management and Technology, Polytechnic Institute of Leiria, Portugal

P18. Luteolin topical delivery: A comparative in vitro Franz cell and mass balance studies using porcine skin and human epidermis
Jingyi Gu[a], Michael Heinrich[a,c], Bruno Da Silva Sil Dos Santos[a,b], Majella Lane[a]
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c Graduate Institute of Integrated Medicine, College of Chinese Medicine, Chinese Medicine Research Center, China Medical University, Taichung

P19. Development of a transdermal therapeutical system by using biodegradable and biocompatible polymers
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P20. Comparison of plon and Corning Parallel Artificial Membrane Permeation Assay (PAMPA) Models
Jiayi Song, Majella E. Lane
School of Pharmacy, UCL, UK

P21. Unravelling epithelial wound repair by label-free morpho-molecular imaging of cellular dynamics
Viktoria Planz[1], Annika Horchler[1], Pia Katharina Vestweber[1], Maike Windbergs[1]
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P22. Topical Pranoprofen Gel for Pain and Inflammation in Farm Animals
Negar Ahmadi[a], Maria Rincón[b], Ana C. Calpena[a], Joaquim Suñer-Carbó[a], Lilian Sosa[c], Mireya Zelaya[c], Mireia Mallandrich[a]
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b Independent researcher, Spain
c Experimental Center in Bioscience (CENBIO), Universidad Nacional Autónoma de Honduras, Tegucigalpa, Honduras

P23. Ultrasound-compatible 3D-printed Franz Diffusion System for Sonophoresis with Microbubbles
Xin Chen[a], Majella Lane[a], Bruno Da Silva Sil Dos Santos[b], Dario Carugo[c]
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P24. The study of interaction between the skin barrier lipids and the corticosteroids through model systems
Filipa de Castro[a], Petra Pullmannová[a], Iva Hrdinová[a], Kateřina Vávrová[a], Andrej Kováčik[a]
a Skin Barrier Research Group, Faculty of Pharmacy in Hradec Králové, Charles University, Hradec Králové, Czech Republic

P25. Accounting for epidermal turnover and binding in dermal absorption predictions
Caitlin Fahrenbruch[a], Tao Chen[a], Neil Morgan[b], Christine Lorez[c], Kieran Moore[b], Natalie Belseya[d]
a Department of Chemical and Process Engineering, University of Surrey, UK
b Syngenta, Jealott's Hill International Research Centre, UK
c Syngenta Crop Protection AG, Switzerland
d Chemical & Biological Sciences Department, National Physical Laboratory, UK

P26. Establishment of a RHE Inflammation Model in vitro and Analysis of Scutellaria Baicalensis, Soy and Germ Extract
Annina Hahn[a], Udo Bock[b], Christiane Kolb[c], Mira Jakobs[c], Alf Lamprecht[a]
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b Bock Project Management, Tawern, Germany
c Bayer Vital GmbH, Leverkusen, Germany

P27. In vivo Evaluation of Prototype for Quantitative Skin Surface Temperature Recording
Udo Bock[a], Dirk Neumann[b]
a Bock Project Management, Tawern, Germany
b Scientific Consilience GmbH, Kleinblittersdorf, Germany

P28. Dosimetry of Limonene as Volatile Organic Chemical in Gas Phase Exposure System for Topical Dosing
Martin Thies[a,b], Sebastian Kollete[a], Udo Bock[a,b]
a Analytical and Ecological Chemistry, Trier University, Trier, Germany
b Environmental Toxicology, Trier University, Trier, Germany

P29. Unveiling the 3D texture of topical semi-solid formulations using micro X-ray computed tomography. The example of bigels
E. Leccia[a], E. Dauphin-Chanard[b], D. Pelisson[b], P. Caisse[b], J. Doucet[a]
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b GATTEFOSSÉ SAS, Saint-Priest, France

P30. Development of lipid nanocapsules for dermal delivery of jak inhibitors
Vendula Janoušková[ab], Eliška Kurfiřtová[a], Barbora Amélie Kindlová[b], Jarmila Zbytovská[a]
a Department of Organic Technology, UCT Prague, Technická 5, 166 28 Prague 6, Czechia
b Zentiva k.s., U Kabelovny 130, 102 37 Prague 10, Czechia

P31. A Regulatory Framework for Bioequivalence Assessment of Topical Drugs
Marta Agostinho Cordeiro[a,b], Margarida Miranda[c], Carla Vitorino[a,b], João José Sousa[a,b]
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b Coimbra Chemistry Centre, Institute of Molecular Sciences, Department of Chemistry, Coimbra, Portugal
c Egas Moniz Center for Interdisciplinary Research, Caparica, Portugal

P32. In vitro release test development for arbutin-loaded chitosan/hyaluronic acid polyelectrolyte complex films for cosmetic use
Ana Ćirić[a], Željana Radonić[b], Jelena Milinković Budinčić[b], Lidija Petrović[b], Milica Lukić[a], Ljiljana Đekić[a]
a Department of Pharmaceutical Technology and Cosmetology, University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia
b Department of Biotechnology and Pharmaceutical Engineering, University of Novi Sad – Faculty of Technology Novi Sad, Novi Sad, Serbia

P33. Cryo Emulsiongel Patches: Influence of the Oil Type on Emulsion Stability and Dermal Drug Delivery
Y. Wiedemann, D. Lunter
Department of Pharmaceutcial Technology and Biopharmacy, University of Tuebingen, Germany

P34. Nanoparticulate systems for topical delivery of Itraconazole
Damla Orhan[a,b], Stanislav Chvíla[a,b], Josef Beránek[b], Jarmila Zbytovská[a]
a Department of Organic Technology, University of Chemisty and Technology Prague, Prague, Czech Republic
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P35. Cutaneous and Follicular Delivery of Bioactives from Natural Plant Extracts using Nanoemulsions: A Case Study using Rice Bran Oil
Erga Syafitri[a,b], Aka Yoann-André Kouassi[a,b], Claudia Prezioso[c], Yogeshvar Kalia[a,b]
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b Institute of Pharmaceutical Sciences of Western Switzerland, University of Geneva, Geneva, Switzerland
c Department of Food and Drug, Università degli Studi di Parma, Parma, Italy

P36. Enhancing formulation substantivity using silicone resins
K. Jehnen, D. Lunter
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P37. In vitro permeation studies of metronidazole in porcine skin
Chunrui Ji, Majella Lane
UCL School of Pharmacy, London, UK.

P38. Bicontinuous cubic mesophases for epicutaneous patch testing of contact allergy
Stella Prastitou[a,b], Emelie J. Nilsson[a,b], Maryam Ahmed Ali[a], Wedad Abhomede[a], Sebastian Björklund[a,b], Johan Engblom
a Department of Biomedical Science, Faculty of Health and Society, Malmö University, Malmö, Sweden
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P39. Effects of fractional laser ablation on gene transcription in viable human skin explants
Si Gou[a,b], Christy Abi Nahed[c], Denis Salomon[d], Hans-Joachim Laubach[e,f], Yogeshvar N. Kalia[a,b] *
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e Division of Dermatology, Geneva University Hospital, 1205 Geneva, Switzerland.
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P40. Natural product-based thermotropic liquid crystals for anti-infective skin treatments
Mariia Nesterkina[a], Iryna Kravchenko[a], Anna K.H. Hirsch[a b], Claus-Michael Lehr[a b]
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b Department of Pharmacy, Saarland University, Saarbrücken, Germany

P41. Effects of styrene oligomers on stratum corneum lipid model membrane
Ajit Kumar Pratihast[a], Georgios Paraskevopoulos[a], Kateřina Vávrová[a]
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P42. Improving Photodynamic Skin Cancer Therapy by Increased Oxygenation
Sofia Fureby[a,b], Tautgirdas Ruzgas[a,b], Emelie J. Nilsson[a,b], Sanja Bulut[c], Adam Clauss[a,b],d, Chris Andersson[e], Johan Engblom[a,b], Sebastian Björklund[a,b]
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c Bioglan AB, Malmö, Sweden
d Clauss Science Support AB, Flyinge, Sweden
e Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

P43. Solvent-free Development of TPGS nanomicelles for Follicular Delivery of Spironolactone
Jonathan Faro Barros[a,b], Zhehao Cui[a,b], Yogeshvar N. Kalia[a,b]
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P44. Influence of excipients on tin fluoride (SnF2) uptake in the TR146 model
Storay Amiri[a] , Christopher J Morris[a], Robert Lucas[b], Majella E. Lane[a]
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b Haleon Consumer Health, The Heath, St Georges Avenue, Weybridge, KT13 0DE, United Kingdom

P45. Investigation of functional properties and antibacterial activity of chitosan–clay composite films with tetracycline-hydrochloride
Danina Krajišnik[a], Snežana Uskoković-Marković[b], Milena Pantić[c], Aleksandra Ilić[c], Aleksandra Daković[d], Ljiljana Djekić[a], Milica Lukić[a]
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c Institute for Food Technology and Biochemistry, Faculty of Agriculture, University of Belgrade, Serbia
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P46. From Aggregation to Activity: Developing a Topical Enzyme Replacement Therapy for a Rare Skin Disease
Paul, K.[a]; Bodes, J.[b]; Traupe, H.[b]; Jose, J.[c]; Langer, K.[a]
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c Institute of Pharmaceutical and Medicinal Chemistry, University of Münster, 48149 Münster, Germany

P47. Potential of two innovative acrylate derivatives for gelation of fragile low-energy nanoemulsions
Anđela Tošić, Jovana Jagodić, Snežana Savić, Ivana Pantelić
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P48. Influence of Ethanol as a Preservative in Topical Formulation on the Dermal Penetration Efficacy of Active Compounds in Healthy and Barrier-Disrupted Skin
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P49. Preformulation and Characterisation of Nifedipine for Topical Drug Delivery Purpose
Zihan Yang 1[a], Majella Lane 2[a], Bruno Da Silva Sil Dos Santos 3[b]
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P50. Impact of Mutations in Surface-Exposed Residues on the Anodal Iontophoretic Delivery of Negatively Charged Nanobodies
Tess Vouillamoz[a], Yogeshvar N. Kalia[a]
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P51. Clinical evaluation of skincare products containing turmeric extract: Potential application in managing radiation-induced dermatitis.
Justyna Dąbrowska[1], Bartłomiej Kubiak[1] ,
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P52. Merging SLNs and Ionic Liquids in Semisolid Matrices: Boosting Skin Delivery of Ferulic Acid
Ana Júlio[a], Carlos Ventura[b], Madalena Batista[c], Mariana Rodrigues[c], Margarida Caroço[c], Filipa Silva[c], José Parreira[c], Luís Oliveira[c], Marta Matos[c], Raquel Mendes[c], João Henriques[c], Ana Sofia Fernandes[a], Nuno Saraiva[a], Catarina Pereira-Leite[a,d], Catarina Rosado[a]
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d LAQV, REQUIMTE, Universidade do Porto, Porto, Portugal.

P53. Entoingredients: the future of skin care?
Catarina Rosado[a], Matilde Liu[a,b], Francisca Marques[a,c], Anurag Choudhury[a,d], Ana Júlio[a], Catarina Pereira-Leite[a,e]
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P54. Exploring the safety and efficacy of an upcycled Humulus lupulus extract for cosmetic applications in Atopic Dermatitis
Ana Rita Gama[a,b], Carolina Gomes[a,b], Ana Sofia Oliveira[a,b], Joana Rolo[a,b], Íris Amado[c], Jorge Pereira[c]; José Martinez-de-Oliveira[a,b], Carmen Lisboa[d,e,] Ana Palmeira-de-Oliveira[a,b,f], Rita Palmeira-de-Oliveira[a,b,f]
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e ULS São João, Department of Dermatology and Venereology, Porto
f Labfit-HPRD Health Products Research and Development, Lda, Covilhã, Portugal

P55. Effective topical treatment of skin inflammatory diseases assisted by photoacoustic waves
Sofia Melo-Guímaro[a,b], João Santos[b], Celso P. João[b], Luís G. Arnaut[a,b], Carlos Serpa[a,b]
a CQC-IMS, Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal
b LaserLeap Technologies, 3025-307 Coimbra, Portugal

P56. Perilla Leaf-Derived Extracellular Vesicle-Like Particles: A Green and Scalable Natural Ingredient for Topical Anti-inflammatory Therapy and Cosmetic Applications
Yali Liu1[a], Shanmin Tao 2[a], Zhengwei Zhang 3[a], Dominique Lunter 4[b], Peng Cao 5[a]
a State Key Laboratory of Technologies for Chinese Medicine Pharmaceutical Process Control and Intelligent Manufacture, Nanjing University of Chinese Medicine, Nanjing 210023, China
a Department of Pharmaceutical Technology, Faculty of Science, Eberhard Karls Universität Tübingen, Auf der Morgenstelle 8, 72076 Tuebingen, Germany

P57. Combining two biophysical techniques to substantiate the anti-aging claims of skin care products: AFM and SAXS coupling
E. Leccia, J. Doucet
NOVITOM SAS, Les Ulis, France

P58. Unveiling the impact of topical formulations on the organization of stratum corneum lipid barrier using X-ray micro-diffraction
E. Leccia, D. Rosa Nunes, J. Doucet
NOVITOM SAS, Les Ulis, France

P59. Developing New Methods to Evaluate the Crystallinity and Solubility Behaviour of Estradiol in Pressure-Sensitive Adhesives
Ryan Maguire[1], Sonja Vucen[1,2], Patrick O'Dwyer[1]
1 Department of Pharmaceutics, School of Pharmacy, University College Cork, Cork
2 SSPC Research Ireland Centre for Pharmaceuticals, School of Pharmacy, University College Cork, Cork, Ireland

P60. In vivo Raman imaging of the skin
P.J. Caspers, C. Nico, T.C. Bakker Schut, G.J. Puppels
RiverD International B.V., Rotterdam, The Netherlands

P61. Catechol-Based Nanocarriers for Targeted Delivery of Tofacitinib in Alopecia Areata: Enhancing Stability and Encapsulation for Skin Applications.
Fabiana Nador, Brigitta Loretz, Claus-Michael Lehr
Department Drug Delivery across Biological Barriers, Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Saarbrücken, Germany

P62. Development of an antimycotic hydrogel using Quality by Design for the treatment of fungal infections
Pintea Andrada[1], Vlad Robert-Alexandru[1], Paula Antonoaea[1], Ciurba Adriana[1]
1 Faculty of Pharmacy, University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania

P63. Imiquimod nanosystems for advanced dermal delivery
Eliška Kurfiřtová[a], Stanislav Chvíla[b], and Jarmila Zbytovská[a]
a Faculty of Chemical Technology, University of Chemistry and Technology, Prague, Czech Republic
b Faculty of Chemical Engineering, University of Chemistry and Technology, Prague, Czech Republic

P64. Hydrogels, oleogels, or bigels for topical application?
Cezara Pintea[1], Vlad Robert-Alexandru[1], Ciurba Adriana[1]
1-Pharmaceutical Technology and Cosmetology Department, Faculty of Pharmacy, University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania

P65. Evaluation of the antioxidant capacity of a gel with lavender oil and orchid extract intended for atopic dermatitis
Shakiba[a], Mireia Mallandrich[b], Camila Folle[ab]
a University International of Catalunya, Sant Cugat del Vallès, Barcelona, Spain.
b Department of Pharmacy, Pharmaceutical Technology and Physical Chemistry, University of Barcelona, Barcelona, Spain.

P66. A Closer Look at Variability in In Vitro Permeation Tests: An Analysis Based on a Caffeine Example
Laura Krumpholz[a,b], Sebastian Polak[c,d], Barbara Wiśniowska[a]
a Department of Social Pharmacy, Unit of Pharmacoepidemiology and Pharmacoeconomics, Faculty of Pharmacy, Jagiellonian University Medical College, Medyczna 9, 30-688 Kraków, Poland
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P67. Assessment of the permeation of an olive oil-based formulation with baricitinib for alopecia areata
Negar Beirampour[a], Ana Cristina Calpena[a], Maria José Rodríguez-Lagunas[b], Beatriz Clares-Naveros[c], Maria Nuria Romero-Olid[d], Mireia Mallandrich[a]
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P68. Rethinking Skincare: Phospholipid-Based Lamellar Systems Promote Accelerated Epidermal Barrier Repair – Results of a Pilot Study
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P69. Topical liposomes loaded with Cannonau pomace extract and quercetin: a sustainable approach for Psoriasis treatment
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P70. Impact of hydrophilic natural deep eutectic solvents on the properties and sensory attributes of carboxymethylcellulose-based hydrogels for skin application

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P71. Optimization of lipid extraction from the stratum corneum (SC)

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P72. A systematic, fast, and miniaturized approach to compound selection for topical delivery

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P73. Optimization of Vasoconstrictor Assay for Evaluation of Bioequivalence of 0.1% Mometasone Furoate Ointment

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Abstracts of poster presentations

P01. Exploring the potential of plant hydrolates in green cosmetic formulations: case study of Pannonian thyme hydrolate

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The aim of this work was to investigate the potential of plant hydrolate to be used as multifunctional ingredient in cosmetic product, emphasizing their environmental and skin-enhancing benefits. Specifically, the work focused on the hydrolate derived from Pannonian thyme (Thymus pannonicus All., Lamiaceae) and additionally the effect of different manufacturing processes was evaluated.
For this purpose, two sets of creams with different emulsifiers were prepared with and without heating. In each set an aqueous phase containing purified water or Pannonian thyme hydrolate was prepared. Formulations with hydrolate were made with and without preservatives and, due to high pH, with and without pH adjustment for performance study. Physicochemical tests (pH and conductivity measurements, continual and oscillatory rheology, antioxidant activity) were carried out and a short-term in vivo study was conducted to test the cosmetic performance. In addition, microbiological quality was tested after 7 days and after 3 months.
Our findings revealed that variations in the aqueous phase did not significantly alter the pH or conductivity of the creams, nor did they affect rheological flow behavior, particularly in formulations prepared without heating. Interestingly, creams made with heating exhibited a wider linear viscoelastic region when hydrolate was included, indicating enhanced stability compared to those made with purified water. Measurements of the stratum corneum moisture highlighted that creams containing hydrolate provided prolonged hydration compared to their water-based counterparts, with the effect being more pronounced by the heated formulations. This enhancement in creams manufactured by heating is likely attributable to the unique emulsifiers and its stabilization methods employed. The short-term study indicated that the creams did not adversely affect the skin pH or barrier integrity. Additionally, the antioxidant properties of Pannonian thyme hydrolate were preserved in both heated and unheated creams, while preservative-free formulations with hydrolate maintained their microbiological quality.
In conclusion, replacing purified water with plant hydrolate not only stabilizes the formulation but also enhances antioxidant activity and skin benefits. This research underscores the potential of hydrolates as multifunctional active ingredients, paving the way for the development of self-preserving, eco-friendly cosmetic products that align with the principles of green chemistry.

P02. Evaluation of natural waterless face cleansers: physicochemical properties and performance assessment

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This study evaluates the physicochemical properties and performance of natural, waterless facial cleansers, focusing on their sustainability and efficacy. The cleansers were prepared using a combination of emollients (avocado butter 3–6%, hydrosoluble cottonseed oil 10–15%, squalane up to 100%), humectant (pentylene glycol 5%), surfactants (sorbitan stearate 3–5%, sorbitan oleate 3–5%, polyglyceryl 10-laurate 1–3%, coco glucoside 10–20%), thickeners (brassica alcohol 1.5–5%, C10-18 triglycerides 1.5–5%) and an antioxidant (tocopherol mix 0.5%). Some formulations also contained lactic acid (0.7%) to adjust pH. The formulations were assessed through various physicochemical analyses and all formulations were analyzed 3 days post-preparation. pH and conductivity were measured after homogenizing 3 g of each formulation with 1 mL and 30 mL of purified water. Rheology was evaluated using a cone/plate system (controlled shear rate procedure, shear rate range 0–200 s^{-1}). The spreadability was tested by placing 0.1 g of the sample on a glass, applying 50 g for 5 minutes and measuring the spread diameter. Water washability was evaluated by applying 0.05 g of the sample to a glass slide or PVC oilcloth, washing with 50 mL of purified water and calculating the residue removal. All formulations exhibited shear-thinning behavior, facilitating easy application. The formulations with a higher thickener content (≥2.5% each) showed higher viscosity but lower spreadability, while formulations with a lower surfactant content (especially those with 10% of coco glucoside) showed lower cleaning efficacy (lower conductivity and washability). Lactic acid significantly influenced the pH, lowering it to 4.41–4.80, which is favorable for skin compatibility. Formulations without lactic acid had a higher pH (7.48–9.18), making them less suitable for sensitive skin. Optimized formulations with 1.5% or 2% of both thickeners showed ideal pH, moderate conductivity (759–798.5 µS/cm), optimal viscosity (maximum apparent viscosity 3365–4235 mPa·s at 5.13 s^{-1}), excellent spreadability (37.8–39.5 mm) and washability (34.8–45.5% removal on glass, and 39.6–43.1% on PVC oilcloth). These results underline the potential of these formulations as sustainable skin care products, ensuring a balance between stability, usability and water efficiency for future commercial applications.

P03. Application of PBPK modelling to optimise IVPT study design and predict the impact of formulation changes on skin permeation

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In vitro permeation testing (IVPT) has been used to assess skin permeation of topical drug products in both industry and academia. To ensure results derived from such studies can address specific questions, studies must be carefully designed, taking into consideration critical factors such as the dose of the product used, selection of receptor solution in relation to sink conditions, sampling frequency, etc. In this work, dermal PBPK (physiologically based pharmacokinetic) modelling was used to aid the design of IVPT studies for Dermovate (clobetasol propionate, CbP) topical cream, 0.05%. The model was first validated by simulating the IVPT study data reported in Lehman et al. 2014. Sensitivity analysis was conducted to assess the impact of CbP receptor solution solubility on skin permeation in vitro. Results showed increased permeation with increased solubility up to 1 – 2 mg/mL, (saturation solubility of clobetasol propionate in the PBS alone is 0.07 mg/ml) beyond which no significant change occurred. Simulations also compared aliquot sampling versus full receptor replacement using different sampling frequencies to determine the optimal sampling volume for quantifiable drug levels in the IVPT study. To confirm the sensitivity analysis results, IVPT studies were conducted using receptor solutions with low, medium, and high CbP solubility. For these studies, simulations described the observed cumulative permeated amounts well: the predicted-to-observed ratios ranged from 1.05 to 1.88, and for skin retention, from 1.57 to 2.33, for all three solubility scenarios. The simulations accurately predicted that sink conditions were not achieved in the lower solubility receptor solution. Additionally, customized in vitro release and IVPT studies, using a generic membrane and skin, respectively, were conducted using in-house CbP creams with varying dispersed phase globule sizes. The model accurately predicted higher release and permeation from formulations with smaller globule sizes, consistent with experimental observations. To conclude, by accurately simulating the impact of factors such as receptor solution solubility, sampling volume, sampling frequency, PBPK models are valuable tools for optimising the design of IVPT studies. The model also predicted changes in skin absorption due to variation in formulation Q3 parameters, providing insights for the development of topical drug products. This case study underscores the role of mechanistic modelling in developing and evaluating topical products applied to the skin.

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P04. A Pivotal, Dermal, In-Vivo Bioequivalence Study performed by Confocal Raman Spectroscopy (CRS)

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Starting from April 2025 the stratum corneum (SC) sampling technique (Tape Stripping, TS), according to the most recent EMA Guideline on quality and equivalence of locally applied, locally acting cutaneous products, can be used in lieu of an expensive and time-consuming clinical endpoint study[1]. However, alternative methods, like CRS are not yet approved. As we believe that CRS, with its microscale resolution and ease of use[2], is the superior method for future dermal bioequivalence studies, we performed a pivotal dermal bioequivalence study to demonstrate the suitability of CRS. Altogether 12 subjects with an age of 49.8 ± 10.3 years and healthy skin were recruited by SGS proderm GmbH (Hamburg, Germany). Four cosmetical products containing salicylic acid (SA) were applied (15 mg product/cm²) to the treatment areas (4 x 6 cm) which were measured by CRS and compared at two time points (1 hr uptake and 4 hr clearance). The measurements with a depth of 0-20 µm, a step size of 2 µm and an integration time of 5 s of the SC fingerprint region (400 – 1800 cm−1) were performed with the 785 nm laser of the Gen2 SCA Ultimate (RiverD International B.V., Rotterdam, Netherlands) Raman device. SA concentration profiles versus SC depth were obtained by the established fitting algorithm[3] of the SkinTools software (RiverD) and used for further bioequivalence calculations described by the EMA[1, 4]. Comparison of the supposedly bioequivalent products not only showed a clear similarity in terms of the obtained SA penetration profiles but also in terms of the penetrated SA amounts into the SC. Since the within-subject variability of the reference product in the study exceeded 50 % in some volunteers and all other requirements of the EMA Guideline on the Investigation of Bioequivalence[4] were met, the acceptance interval was widened from 80.00 – 125.00 % to 69.84 – 143.19 %. Taking this into account, the 90 % confidence intervals of the supposedly bioequivalent products were within the acceptance interval for both time points, while those of the control product were completely outside this range. With respect to the Guideline on quality and equivalence of locally applied, locally acting cutaneous products[1], these results show that the bioequivalence study is valid and that the test product can be classified as bioequivalent to the reference product. This study should be seen as proof of CRS suitability for dermal bioequivalence investigation, which is why the method deserves to be included in the subsequent version of the EMA Guideline on quality and equivalence of locally applied, locally acting cutaneous products.

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P05. Topical delivery of terbinafine: In-vivo studies

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Skin fungal infections are the most common skin disease form affecting our healthy daily life. There is substantial variation in the approaches used for the treatment of fungal infections of the skin, but none of these options delivers optimum clinical outcomes. For effective treatment, the drug should act at the site of infection with minimal systemic exposure. Previously, the development of different prototype single, binary, ternary and quaternary formulations was described, and their efficacy was examined in porcine skin and human skin. In the present work a finite dose (15 µL/3.8 cm2) in-vivo evaluation of the most promising 1% (w/w) TBF formulations and commercial preparations in human volunteers is reported using Confocal Raman Spectroscopy (CRS). The selected formulations were: PG:IPA (50:50), PG:TC (75:25), IPM:PG:IPA (10:55:35), PG:TC:IPA (60:20:20), IPM:PG:TC:IPA (10:40:40:10) and IPM:PG:PEG 200:IPA (10:30:30:30). Subsequently, in vivo skin uptake of TBF from the two best formulations: PG:TC:IPA (60:20:20) and IPM:PG:TC:IPA (10:40:40:10) was also studied using sequential tape stripping with six volunteers. The results of the finite dose in-vivo normalised depth profiles of six different novel 1% (w/w) TBF formulations and a commercial gel preparation indicated that most of the TBF-free base of the novel formulations remains in the SC after 4 h application and some TBF is detectable in the viable epidermis to a smaller extent. On the other hand, the commercial TBF formulation allowed TBF penetration of 67% of the total thickness of SC at 4 h. The results of tape stripping of PG:TC:IPA (60:20:20) and IPM:PG:TC:IPA (10:40:40:10) formulations confirmed that TBF could be detected in up to 20 tapes for both formulations. The amount of TBF for the PG:TC:IPA (60:20:20) formulation was significantly higher than the IPM:PG:TC:IPA (10:40:40:10) formulations ($p < 0.05$) for all tapes except tape 1. The data also confirm the availability of the drug at the site of action for the PG:TC:IPA (60:20:20) and IPM:PG:TC:IPA (10:40:40:10) formulations. The next stages of the work will focus on development of TBF gel preparations using optimised solvent systems that will be evaluated for efficacy using in-vivo human studies.

P06. Bioadhesive chitosan films loading curcumin for safe and effective skin cancer topical treatment

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Abstract: Curcumin is a natural polyphenol that has shown effect against tumoral cells. However, it presents challenging physicochemical features, including high lipophilicity and instability in physiological pH, resulting in low oral bioavailability and poor skin permeation. These challenges highlight the need for alternative administration routes and adequate pharmaceutical forms for targeted curcumin application. Thus, this study proposes chitosan-based bioadhesive films to facilitate the topical delivery of curcumin in skin cancer treatment. The films, which incorporated curcumin, were formulated using varying proportions of chitosan, polyvinyl alcohol, Poloxamer® 407, and propylene glycol. These films were assessed in vitro for stability, drug release, skin permeation, cell viability (with and without radiotherapy), and skin irritation (HET-CAM assay). The three selected films with different compositions demonstrated physical stability and preserved curcumin content at room temperature for 90 days. Drug release was effectively controlled during the first 8 hours, with release rates ranging from 51.6 ± 4.8% to 65.6 ± 13.0% depending on the evaluated film. The films also enhanced drug penetration into the skin (stratum corneum: 1.3 ± 0.1 to 1.9 ± 0.8 μg/cm²; deeper skin layers: 1.7 ± 0.1 to 2.7 ± 0.2 μg/cm²) compared to a curcumin control solution, which provided negligible curcumin skin absorption. A cytotoxicity test on metastatic melanoma cells showed that curcumin at topical doses exerted activity similar to that delivered via the skin. Furthermore, curcumin alone was more effective in inhibiting tumor cells growth than radiotherapy alone ($p<0.01$), with no additional benefit observed when curcumin was combined with radiotherapy. Finally, irritation tests confirmed that the films were safe for topical application. Therefore, the developed chitosan-based bioadhesive films may represent a promising alternative for the topical treatment of skin tumors using curcumin.

P07. Influence of nanoparticles'characteristics on iontophoretic targeted deposition to the hair follicles

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Abstract: Hair follicles (HFs) serve as a promising pathway for drug delivery aimed at addressing various skin disorders. Nanoparticles (NPs) have been used for targeting HFs, as they can preferentially accumulate within these structures Iontophoresis is a technique that improves the penetration of drugs by applying a gentle electrical current to the formulation. Combining these approaches could yield optimal outcomes, as the HFs may offer a pathway of reduced electrical resistance. However, current literature lacks clarity on the ideal characteristics of NPs for effective iontophoretic drug delivery targeting HFs. In this study, we sought to investigate how the size and surface charge of gelatin NPs influence their deposition into HFs when iontophoresis is applied. For this, four formulations of gelatin NPs were developed with varying concentrations and polymer types—positively charged type A and negatively charged type B—resulting in sizes between 220 nm and 770 nm. To monitor NP deposition, we encapsulated the fluorescent dye TRITC-dextran 150 kDa within the NPs. We conducted in vitro cutaneous penetration experiments using pig ear skin with and without iontophoresis over a duration of six hours. The deposition profiles were analyzed using confocal laser scanning microscopy. Our results revealed that the larger positively charged NPs (designated as AL) exhibited significantly higher accumulation in the deeper regions of the HFs. Notably, application of iontophoresis led to a substantial increase in NP deposition, resulting in the strongest fluorescent signal observed. This indicates that both the size and charge of NPs play critical roles in enhancing their deposition into HFs, particularly under the influence of electrical current. Thus, our findings illuminate valuable insights into the utilization of NPs in drug delivery systems, opening up new avenues for the treatment of various conditions affecting hair follicles.

P08. Characterization of Cimetidine for Topical Delivery

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Background
Cimetidine, a histamine-2 receptor antagonist primarily used to treat gastrointestinal disorders, exhibits immunomodulatory potential for treating cutaneous warts. Compared to traditional oral or intravenous administration, topical delivery could enhance efficacy by directly targeting affected tissues and avoiding first-pass metabolism. However, research on topical cimetidine formulations remains limited, highlighting a critical need for further investigation. This study aimed to [(1)] develop a validated HPLC analytical method for cimetidine and [(2)] characterise its physicochemical properties, including degradation temperature, melting point, distribution coefficient (LogD), solubility and stability in pharmaceutical solvents.
Methods
An HPLC method of cimetidine was validated according to ICH guidelines. Thermal properties were assessed via thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). LogD (pH 7.4) was determined using the shake flask method (OECD guideline). Solubility was tested in twenty-one single solvents, and stability was evaluated in nine selected solvents over 72 h across varying concentrations (32 ± 1°C, n=3).
Results
The HPLC method demonstrated excellent linearity, accuracy, precision, robustness, and system suitability, with LOD and LOQ values of 0.145 µg/mL and 0.439 µg/mL, respectively. Cimetidine exhibited a degradation temperature of 262.67 °C and a melting point of 140.02 °C. LogD1-octanol/PBS was 0.33 ± 0.02. Maximum solubility was observed in PEG 200 (137.68 ± 3.89 mg/mL) and PG (103.11 ± 1.05 mg/mL), while minimal solubility (<0.01 mg/mL) occurred in IPM and IPP. Cimetidine remained stable in all tested solvents except oleic acid, which reduced recovery to 57.23% after 72 hours.
Conclusion
This study established a validated HPLC method and successfully characterised the physicochemical properties of cimetidine. Candidate solvents were screened for solubility and stability. These findings provide a foundation for developing novel topical cimetidine formulations to enhance cutaneous delivery efficacy. Future work will focus on formulation optimisation and skin permeation evaluation.

P09. Dermal delivery of phytochemicals: Release of ginsenosides from topical formulations with Korean red ginseng extract ex vivo

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Abstract
Antioxidant Korean red ginseng (KRG) extract is often used in dermal preparations to counteract ultraviolet (UV)-induced oxidative stress leading to damage of skin cells and further to development of skin cancer. However, formulation strategies are scarce, and proof of concept is still a miss, whether main ingredients such as ginsenosides with high molecular weight (approximately 1000 g/mol) can cross the stratum corneum.
Our research group has so far investigated permeation potential of ginsenosides from optimized KRG preparations such as oil-in-water nanoemulsions (NEs) and hydroalcoholic gels using porcine skin: results showed permeation potential of both vehicle types, particularly for the moderately lipophilic Rg1, with gels showing superior performance.
In the present work, release studies of ginsenosides were performed via Franz-type diffusion cells using synthetic cellulose membranes to evaluate compound solubility of extract ingredients and their release from different vehicles. Quantification was conducted by ultra-high-performance liquid chromatography coupled with mass spectrometry (UHPLC/MS). Both ginsenosides Rg1 and Rb1 (more hydrophilic) were able to permeate the membrane after 24 hours. As for permeation experiments, gels demonstrated higher release of ginsenosides compared to NEs.
Current studies will serve to obtain methodological knowledge for the establishment of standardized measurement protocols of complex multicompounds such as phytochemicals.

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P10. Understanding Skin Barrier Formation: Insights from Lipid Model Systems

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The stratum corneum (SC), the outermost layer of the epidermis, plays a fundamental role in protecting the skin from environmental insults while regulating water loss. This barrier function is governed by a specialized intercellular lipid matrix composed of ceramides (CER), cholesterol (CHOL), and free fatty acids (FFAs), which originate from precursor molecules such as cholesteryl sulfate (CHOL-S), glucosylceramides (GCER), and phospholipids. The enzymatic transformation of these precursors during epidermal differentiation is essential for the development of a competent skin barrier. Defects in this process contribute to skin disorders like atopic dermatitis, where altered lipid composition leads to impaired barrier function and increased water loss.
This study focused on designing lipid model systems that replicate key aspects of SC barrier formation by incorporating both precursor and mature lipids. The models were tailored to reflect physiological conditions, with precursors examined at pH 7.4 (representing the granular layer) and mature barrier lipids at pH 5.5 (mimicking the SC environment). Structural organization was characterized using X-ray diffraction to analyze lamellar arrangements, while infrared spectroscopy provided insights into lateral lipid organization and chain ordering. Permeability assays (water loss, electric impedance, further assessed the barrier properties of the models.
The study revealed that the presence of barrier lipid precursors leads to the loss of long periodicity phase and less ordered lipids. Furthermore, an increased concentration of these precursors resulted in reduced barrier functionality, as evidenced by increased water loss and enhanced permeability to model permeant. The results contribute to a deeper understanding of lipid processing in SC formation and its impact on skin barrier integrity. These findings offer a valuable framework for developing therapeutic formulations designed to restore and enhance barrier function in dermatological conditions associated with lipid deficiencies.
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P11. New aspects about the impact of ceramides to the substructure of the Stratum corneum barrier function

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The main lipid compounds of the outermost layer of human skin are ceramides, free fatty acids and cholesterol. Although numerous studies performed in the past could demonstrate the importance of these lipids for an intact skin barrier function, the knowledge about the impact of each single component on the lamellar lipid films is still lacking. Especially, the ceramides are a very heterogeneous group with high relevance for a proper barrier. It was found that the reason for the high stability of the lamellae is related to the lipid structure and function, with the type and extent of interactions between the head groups of the individual ceramide subspecies being particularly important. Elucidating these at the molecular level could help to understand ceramide phase behavior in general.

Using grazing incidence X-ray diffraction (GIXD) and measurements of Langmuir isotherms, the current work investigated the lateral packing of the monolayers of different subclasses of C18:0 ceramides at air-water interfaces, including phytosphingosine, sphingosine, and dihydrosphingosine ceramides, all with either α-hydroxy and non-hydroxy N-acylated fatty acyl.

We were able to observe clear effects of the minimal differences in the polar head group structures of the sphingoid bases, with respect to the number and position of hydroxyl groups and double bonds, on the ceramide arrangement regarding the compressibility and structure of the films they formed, revealing that the hydroxyl group at the C4 of the phytosphingosine ceramides not only leads to the formation of a hydrogen bond network but also to a stable suprastructure, which might be of high benefit for the barrier properties of intact skin.

P12. Bioequivalence assessment of topical products in focus: A feasibility study and the new EMA Guideline

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The publication of the new European Medicines Agency (EMA) guideline on `Quality and equivalence of locally applied, locally acting cutaneous products` in October 2024 has been long awaited by the pharmaceutical industry and stakeholders. From the date of application in April 2025, the guideline parameters and the test protocols for conducting equivalence tests must be fulfilled for the approval procedure of a newly developed generic product. However, details of the test protocols and the statistical evaluation are still controversial and data on the quality and evidence of the proposed test conditions are scarce.

In this study, we conducted an in vitro performance test (IVPT) based on the specifications of the EMA draft guideline, which corresponded to those of the final version. Two approved topical products, whose therapeutic equivalence had already been proven by clinical studies during the approval process, were tested and compared for their equivalence in penetration and permeation behaviour on human ex vivo skin. The complex biometric data processing revealed that in vitro equivalence could not be established for all skin areas for both the reference product and the generic product. In addition, the necessity of the negative control proposed in the guideline must be regarded as questionable in view of the results presented.

Finally, there were indications that a lower number of skin donors would be sufficient to achieve statistically significant equivalence when comparing all formulations used. Here, n=7 donors were proposed instead of n≥12 as required by the EMA guideline, which simultaneously reduces the level of biodiversity. In addition, a higher number of independent replicates (n>2) is proposed for adequate statistics.

P13. A clinical dermal open flow microperfusion (dOFM) study to assess bioequivalence (BE) of different topically applied diclofenac products

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In several previously performed clinical studies, the cutaneous sampling technology known as dermal open flow microperfusion (dOFM) has successfully demonstrated its capability to accurately and sensitively compare the cutaneous pharmacokinetic (PK) of various topically applied drug products (from hydrophilic to moderate lipophilic and moderate protein-bound drugs) for bioequivalence (BE) evaluations.[1,2]
To evaluate dOFM's capability to assess BE of highly lipophilic and highly protein-bound drugs, we performed a clinical study using several products containing diclofenac sodium. This study comprised of a pilot study (n = 6) and a subsequent pivotal study (n = 16). The pilot study aimed to determine the optimal study design parameters for the pivotal study. The objective of the pivotal study was to assess BE by comparing the cutaneous PK of the reference diclofenac sodium topical gel, 1% with those from its approved generic gel product (positive BE control), and those from diclofenac sodium topical solution, 2% (negative BE control).
In the pilot study, dOFM successfully differentiated the drug bioavailability from different doses of the reference gel (2, 10 and 50 mg/cm²) and the design parameters for the pivotal study were determined. The results from the pivotal study showed that the drug bioavailability from the negative control was sensitively discriminated from that for the reference gel and the product was found not to be bioequivalent. That being said, the non-equivalent solution showed an order of magnitude higher diclofenac bioavailability compared to gel formulations that led to lateral diffusion of diclofenac to the adjacent dOFM probes under the sites treated with the reference gel. An additional sensitivity analysis demonstrated that only the data from the nearest dOFM probe of the adjacent application site was impacted by lateral diffusion and was thus, excluded prior to BE-analysis. When anomalous data were excluded, dOFM could accurately establish BE of the generic gel (positive control for) to its reference.
These results for diclofenac and those from prior studies indicate that dOFM has the potential to support a demonstration of BE for a wide range of different topical drug products. Understanding the potential impact of local crosstalk, in general, and during pilot studies, can help to optimize the study design of pivotal BE studies.

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P14. Assessment of Skin Permeation using Stimulated Raman Scattering Imaging and In-Silico Modelling

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Understanding the mechanisms governing skin permeation is essential for developing safe and effective topical drug delivery systems and skincare products. This study investigates the partitioning behaviour of six model permeants: palmitic acid, terbinafine, 4-cyanophenol, fumaric acid, caffeine and propylene glycol into human skin. It focussed on the two primary penetration pathways: the intercellular lipid matrix and intracellular corneocyte cells. Using stimulated Raman scattering (SRS) microscopy, a label-free optical imaging technique with subcellular resolution, we examined the distribution of permeants within the stratum corneum (SC). Lipophilic compounds exhibited a strong affinity for the intercellular lipid matrix, with partitioning increasing with lipophilicity, while hydrophilic molecules preferentially localized in corneocytes, with affinity rising with hydrophilicity. Depth-stack SRS imaging of 4-cyanophenol and caffeine revealed distinct concentration-depth profiles, with 4-cyanophenol showing a monotonic decrease while caffeine displaying a depth-dependent diffusion reflective of the SC's anisotropic structure. These experimental insights were integrated into an in-silico mechanistic model, improving its accuracy by refining solute partitioning and diffusion coefficients. Additionally, propylene glycol was quantified as a permeation enhancer, increasing the permeation flux of 4-cyanophenol and caffeine by factors of 1.30 and 1.06, respectively, compared to aqueous vehicles. By combining high-resolution experimental data with computational modelling, this work advances our understanding of skin permeation mechanisms and establishes a robust framework for the systematic evaluation of topical drug delivery systems.

P15. Innovate in topical: sprayable vehicles for patient-friendly treatments

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Sprayability can be a significant feature for topical drug development, from treating skin lesions without direct contact to facilitating product application on large or hard-to-reach body surface areas. However, only a limited number of sprayable drugs are available on the market, with formulation possibilities being severely limited by the lack of polymers able to combine suitable fluidity and required stability. This work evaluated the sprayability and formulation performance of a novel polymer hydroxyethyl acrylate / sodium acryloyldimethyl taurate copolymer in aqueous gels and O/W emulsions. Comparison was done to the only polymer listed in the FDA's Inactive Ingredient Database hydroxyethyl cellulose of low-molecular weight[(1)]. Gel & O/W emulsions were developed with increasing concentration of each polymer. Sprayability was measured through an in-house characterization method (diffusion surface from a standard packaging on a cardboard at a fixed distance, cm^2). Stability of the prototypes was assessed over a 1-month period, with a visual aspect, pH and viscosity follow-up.
Both polymers exhibit a sprayability inversely correlated to their concentration. Surprisingly, hydroxyethyl acrylate / sodium acryloyldimethyl taurate copolymer has demonstrated better sprayability despite higher viscosity of the prototypes. This stronger thickening resulted in better stability of the oil-in-water emulsions compared to the one obtained with hydroxyethyl cellulose. As such, hydroxyethyl acrylate / sodium acryloyldimethyl taurate copolymer shows potential to facilitate the development of new sprayable topical drugs.

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P16. Cerosomes for Advanced Therapy of Inflammatory Skin Diseases

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Inflammatory skin diseases, such as psoriasis or atopic dermatitis, are related to the damaged skin barrier and reduced ceramide levels in the stratum corneum (SC). Direct ceramide administration offers an alternative to corticosteroids but faces challenges due to ceramides´ poor solubility and low bioavailability into the skin. In recent years, we have developed several promising nanoparticulate systems with high efficiency in dermal delivery. One of these systems are cerosomes (CRs), novel vesicular lipid carriers mimicking SC lipid composition, which can effectively deliver ceramides directly into the skin.
Previously, CRs contained only the long-chain ceramides (NP and AP). The current goal is to enhance CRs with the ultra-long chain ceramide EOP. However, the EOP molecule is extremely rigid, crystalline and poorly soluble, so its embedding into the CRs structure is highly challenging. Here, we present new CRs enriched with EOP (EOP-CRs), prepared by thin lipid film hydration. The formulations consisted of ceramides EOP, NP and AP in various ratios in equimolar mixtures with other SC lipids (cholesterol and fatty acids, namely stearic and lignoceric acid).

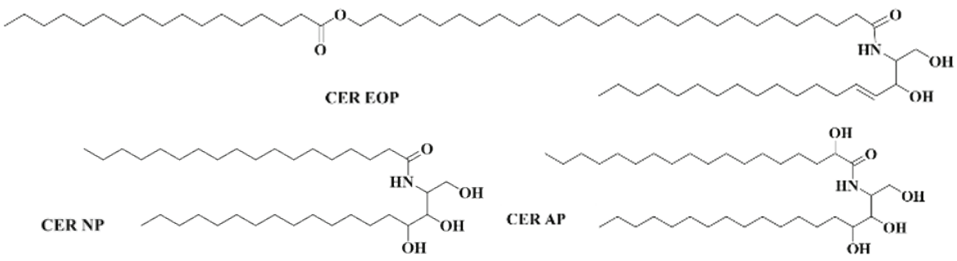

Fig. 1. Chemical structure of ceramides used in the formulation.

EOP-enriched CRs (EOP-CRs) were characterized in terms of size by dynamic light scattering. Their morphology and lipid crystallinity were monitored by optical and transmission electron microscopy. Furthermore, the EOP-CRs efficacy in skin barrier recovery was verified by an ex vivo skin restoration test which used chemically damaged porcine skin as a model of disrupted skin barrier.
EOP-CRs were successfully developed with a total lipid content of 1 %. Their size was around 1 μm. The formulation did not include any crystal fraction. The ex vivo skin restoration study proved the importance of EOP in the formulation compared to commonly used ceramides NP and AP, even at very low concentration (0.07 % in total). In summary, EOP-CRs were found to be successful in skin restoration compared to a simple lipid suspension. This upgraded formulation has high potential to improve treatment of inflammatory skin diseases.

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P17. Shelf life of fresh and frozen skin for in vitro dermal absorption, skin permeation and skin penetration tests

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Ex vivo skin (dermatomed1 and full-thickness2) from healthy donors is used to determine the absorption of substances through the skin barrier. In this way, the local mode of action of chemical substances, drugs and cosmetics can be determined, as well as the bioavailability for the human organism (OECD Guideline 428). Skin is also used in penetration and permeation studies (EMA Guideline 708282/2018) for understanding drug products and its mode of action on the surface of the skin. This requires skin tissue with a functional skin barrier, which can be determined by measuring the Transepidermal water loss (TEWL).
As we ship fresh and cryopreserved ex vivo human tissue samples to our clients worldwide, we need to determine (i) for how long we can store the tissues, (ii) if shipping on dry ice may impair the quality of the discs and (iii) for how many days the skin barrier function can be maintained in fresh tissue.

The TEWL describes the amount of water that is measured on the surface of the skin per hour and per skin area. A damage to the stratum corneum results in high TEWL values. Expected values for a healthy skin barrier function are in a range of 0.5 - 13 g/m2 x h [(1)].
For measuring the TEWL a VapoMeter based on the closed chamber principle was used.
In order to determine the skin barrier function over a storage and transportation period, the TEWL of the skin was measured initially after skin surgery and at various times during the storage at -20 °C (dermatomed skin 300-600µm), 4 °C or room temperature (full thickness skin). For each determination, the skin was clamped in Franz diffusion cells and tempered up to 32 °C for 30 and 60 minutes before measuring the TEWL.

To evaluate if the transport of the tissue samples on dry ice has an effect or not, the experiments for testing the quality of the human skin explants were performed in parallel at Polytechnic Institute of Leiria and at PRIMACYT in Schwerin. TEWL values of frozen skin discs stored at PRIMACYT did not change with time and reached values of 8.7 ± 1.2 g/m2 x h after 6 months (donor 1). The TEWL values of the skin shipped on dry ice to Leiria stored at -20 °C for up to 6 months did not change with time of storage and resulted in a value of 12.4 ± 0.5 g/m2 x h (donor 1) and of 9.9 ± 1.7 g/m2 x h (donor 2) after 6 months. The TEWL of the fresh skin (initial value=5.0 ± 1.0 g/m2 x h), stored in PBS at 4 °C, were measured after 24, 48 and 72 hours and resulted in values of 7.1 ± 0.7 g/m2 x h after 72 hours. For the skin stored at room temperature without any solution the TEWL is 8.3 ± 0.6 g/m2 x h after 72 hours.

In summary, the full thickness skin can be stored at 4 °C and room temperature at least for up to 72 hours without getting a loss in the functionality of the skin barrier. The dermatomed skin can be stored for up to 6 months at -20 °C. Shipment of frozen skin on dry ice has no influence on the skin integrity. Further tests are currently under way to determine if longer storage times are possible.

1 Dermatomed skin = skin with a thinner thickness of 200–1000 µm only including the upper layer of the skin (e.g. epidermis and stratum corneum)
2 Full-thickness skin = Subcutaneous fatty tissue removed but skin not further processed

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P18. Luteolin topical delivery: A comparative in vitro Franz cell and mass balance studies using porcine skin and human epidermis

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Background Luteolin, a naturally occurring flavonoid with anti-inflammatory and antioxidant properties, has shown potential in treating dermatological conditions, such as psoriasis and atopic dermatitis. However, its low aqueous solubility, high melting point, and strong keratin affinity pose significant challenges for effective topical delivery. This study investigates the skin retention of luteolin through in vitro studies. It aims to understand how solvent selection influences luteolin retention in the skin. The study systematically assesses binary and ternary solvent combinations. This work also compares results between human epidermis and porcine skin models.

Methods In vitro Franz cell studies were conducted using vertical Franz diffusion cells with full-thickness porcine skin and human epidermis as permeation membranes. A series of 1% (w/v) luteolin formulations were prepared using selected binary and ternary solvent systems, including Transcutol® P (TC), propylene glycol (PG) and isopropyl myristate (IPM). The solubility, thermodynamic activity, and saturation state of luteolin in these solvent systems were evaluated. Mass balance studies were conducted to quantify luteolin retention in the skin and on the skin surface. The in vitro Franz cell studies were conducted over 24 h, with samples collected at various time points and analyzed using high-performance liquid chromatography (HPLC). Statistical analyses were performed to assess the significance of differences in skin retention across formulations and between human and porcine skin models.

Results No permeation of luteolin through the skin was observed in any of the tested formulations. However, significant differences in skin retention were noted. The binary solvent systems TC/PG (25/75) and TC/IPM (35/65) demonstrated the highest skin retention, with 7.06% and 6.09% of luteolin retained in porcine skin, respectively. Similar trends were observed in human epidermis. Ternary solvent systems, particularly TC/PG/IPM (60/10/30), also showed promising skin retention (6.45% in porcine skin and 5.36% in human epidermis). Comparative studies revealed that porcine skin was more permeable than human epidermis, with higher luteolin retention and lower amounts of the active remaining on the skin surface. A strong correlation ($r^2 = 0.91$) was observed between porcine skin and human epidermis results.

Conclusions This study highlights the importance of solvent selection in optimizing the skin retention of luteolin for topical delivery. Factors such as solubility, saturation state, and solvent composition may influence retention of the active. Overall, these findings provide valuable formulation insights for effective topical delivery of luteolin in dermatological applications. Further in vivo studies to validate these findings will be conducted in the future.

P19. Development of a transdermal therapeutical system by using biodegradable and biocompatible polymers

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Carrageenan-based hydrogels can be a promising alternative to synthetic polymer hydrogels. Due to their excellent swelling properties, biocompatibility and biodegradability, they are an excellent starting material for the development of a transdermal therapeutic systems (TTS). [1]
The most commonly used types of carrageenan in pharmaceutical applications are κ-, ι-, and λ-carrageenan. [2] The mechanical strength of carrageenan-based hydrogels varies depending on the degree of sulfation. It has been observed that λ-carrageenan, with the highest number of sulfate groups, serves primarily as a thickening agent for liquids due to its inability to form polymer network structures. In contrast, ι-carrageenan, with a reduced number of sulfate groups, forms softer gels, while κ-carrageenan, with the least sulfation, produces the strongest but also most brittle gels. [3] For this reason, only κ-carrageenan was selected for the development of a TTS.
The κ-carrageenan gels were optimized for mechanical stability and flexibility by preparing different concentrations of κ-carrageenan. The concentrations of κ-carrageenan were chosen in the range of 2.0% to 5.0% (w/w). Another point that was considered was the treatment with CaCl2 and KCl ions, as the combination of carrageenan with counter ions was described to be a promising way to strengthen the gel network. [4] To investigate the influence of ions concentrations between 50 to 500 mM were chosen. Finally, the combination with other biodegradable polymers, such as pectin, locust bean gum and glucomannan, was evaluated.
The hydrogels were prepared by dissolving the calculated amounts of polymers and ions in deionized water under heat for 1.5 hours. They were then left to stand overnight and afterwards characterized by oscillatory shear rheology.
The results showed that the manufacturing process, addition of ions and combination with other polymers at different concentrations positively influenced the mechanical stability of the gels. Therefore, higher concentrations of κ-carrageenan produced stronger gels but with low elasticity.
For release studies, the hydrogels were loaded with diclofenac sodium as a model drug and tested over an 8-hour period by using synthetic membranes in Franz diffusions cells. The results indicate that modifying κ-carrageenan gels with other polymers enhances their mechanical stability without negatively affecting the release of the active ingredient. Therefore, κ-carrageenan gels represent a promising alternative for the development of new drug delivery systems, such as transdermal therapeutic systems (TTS).

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P20. Comparison of pIon and Corning Parallel Artificial Membrane Permeation Assay (PAMPA) Models

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Purpose
Luteolin is a flavonoid compound that has demonstrated several pharmacological activities including anti-oxidative and anti-inflammatory efficacy. The Parallel Artificial Membrane Permeation Assay (PAMPA) model has been proposed as a high-throughput model for screening of compounds intended for delivery to the skin. The aim of the present work was to investigate the permeation of luteolin in two PAMPA models namely those supplied by Corning (USA) and Pion Inc (USA).

Methods
A number of test formulations were prepared for evaluation in the two PAMPA models. The formulations comprised of Transcutol®P (TC), 1,2-propanediol (PG) and isopropyl myristate (IPM). The stability of luteolin in all formulations was determined over 72 h at 32 ± 0.5 °C. The PAMPA permeation studies were conducted at 32 ± 1 °C. The applied doses were 30 µl and 10 µl. After formulations were applied to donor cells, the PAMPA plates were incubated in a Gut-BoxTM device for 5 h, and at 5, 10, 30, 45, 60, 90, 120, 180, and 240 min, the receptor plates were replaced with new receptor plates. All samples were analyzed with HPLC.

Table 1 Composition of solvent systems evaluated in PAMPA models (concentration: 1%)

Formulation	Composition
A	TC: PG (25: 75)
B	TC: IPM (35: 65)
C	TC: PG: IPM (60: 10: 30)

Results
The percentage recovery values of luteolin in all test vehicles were > 90%. For the 30 µl applied dose, the highest luteolin permeation was observed for formulation A compared with the other formulations in the Corning (32.97±1.77µg/cm2) and Pion (24.13±1.56µg/cm2) models. In the Corning model, the p values between two groups were: A-C: $p \leq 0.001$, A-B: $p \leq 0.001$; in the Pion model, A-C: $p < 0.05$, A-B: $p < 0.05$, confirming that permeation of formulation A was higher than other formulations statistically. For the 10 µl applied dose, the highest permeation was observed for formulation C compared with the other formulations in the Corning (58.75±3.36µg/cm2) and Pion (60.59±2.20µg/cm2) models. In the Corning model, the p values between two groups were: A-C: $p \leq 0.001$, A-B: $p \leq 0.001$, B-C: $p \leq 0.001$; in the Pion model, A-C: $p \leq 0.01$, indicating that formulation C showed statistical differences when compared with the other formulations.

Conclusion
The composition of the solvent systems, the doses applied and the composition of filter membranes of the two types of PAMPA plates are all expected to influence the permeation results. The pIon membrane is composed of cholesterol and ceramide analogues while the Corning membrane comprises phospholipids. The next stage of the work will evaluate luteolin permeation under finite dose conditions.

P21. Unravelling epithelial wound repair by label-free morpho-molecular imaging of cellular dynamics

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Background: Mechanistic insights into epithelial cell dynamics during wound repair are of tremendous importance for deciphering disease mechanisms and advancing the rational development of wound therapeutics. In this study, we employed label-free confocal Raman microscopy (CRM) to investigate the molecular processes driving human epithelial wound healing dynamics from single cell to ex vivo tissue level.
Methods: Excised human skin was utilized to prepare full-thickness punch biopsy wound models. Biomolecular imaging was performed using a confocal Raman microscope equipped with an optical profilometry sensor. For single-cell studies, human keratinocytes were treated with cytochalasin D and mitomycin C to selectively analyse migratory and proliferative epithelial phenotypes.
Results: To study wound healing processes ex vivo, a dual-technique approach based on optical profilometry coupled with CRM was utilized. This method allowed for non-contact, 3D capturing of wound topography while simultaneously tracking surface-contour-guided molecular changes. Raman signals discriminated dermis from epidermis and identified re-epithelialized regions. Interestingly, time-dependent spectral analysis revealed the transition from a single basal cell layer to a stratified epidermis by increased signals of (phospho-)lipids and cholesterol indicating gradual epidermal barrier restoration. In a next step, single-cell studies by human keratinocytes were performed for in-depth analysis of the molecular orchestration of wound healing dynamics with particular focus on cell migration and proliferation. We observed a phenotypic shift of migrating keratinocytes to mesenchymal-like characteristics with a pronounced stellate morphology. The epithelial-mesenchymal transition was accompanied by nuclear translocation enabling leader cell formation at the wound edge to facilitate directed collective movement. In this context, spectral variations in nucleic acid, protein and lipid composition served as key indicators of cellular state and function. Notably, alterations in Raman spectral peaks (e.g. 2936 cm^{-1} / 1448 cm^{-1} ratio) were more pronounced in migratory keratinocytes, reflecting significant cytoskeletal reorganization.
Conclusions: We successfully employed Raman microscopy as powerful tool for label-free biomolecular imaging to gain deeper insights into the intricate cellular processes driving epithelial wound repair, thereby paving the way for future effective therapeutic interventions.

P22. Topical Pranoprofen Gel for Pain and Inflammation in Farm Animals

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Background: Ear tagging is a routine procedure for identifying farm animals, but it can result in pain and stress, raising animal welfare concerns. The use of topical nonsteroidal anti-inflammatory drugs (NSAIDs) has been explored as a method to alleviate this pain without the systemic effects associated with other analgesics. Topical gels formulated with active ingredients like diclofenac sodium have shown efficacy in managing pain and inflammation in various animal models. The aim of the work was to develop a topical gel with pranoprofen to manage pain, inflammation and discomfort during routine invasive procedures to enhance animal welfare. Methods: The gel was prepared at 1.5% of pranoprofen using 18% of poloxamer-188 as gelling agent. The gel formulation was tested for in vitro drug release, an ex vivo permeation study on cow skin was conducted, and the anti-inflammatory capacity of the gel was assessed on ear mice. The study consisted inducing an ear oedema by topical xylol and the ear thickness of the mice was measured. Results: The release of pranoprofen followed a hyperbola model, showing an initial fast released followed by an asymptotic trend. According to the model, half of the drug release was achieved at 23 minutes (kd = 23 min). Regarding the distribution of pranoprofen in the permeation study, the drug was mainly retained in the skin (about 10%) whereas only about 0.5% permeated into the receptor medium. The measurement of ear thickness in a xylol-induced ear oedema model in mice evaluates the anti-inflammatory effects of topical formulations, the degree of ear swelling reflects the extent of inflammation. The gel formulation effectively reduced the ear thickness bringing it to values comparable to the negative control. Conclusions: The low permeation into the receptor medium suggests limited systemic delivery, while the high skin retention could be beneficial for localized therapeutic effects. Additionally, the formulation exhibited anti-inflammatory activity. Hence, Pranoprofen gel is a suitable candidate for targeting inflammation or pain at the application site.

P23. Ultrasound-compatible 3D-printed Franz Diffusion System for Sonophoresis with Microbubbles

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Purpose:
Sonophoresis is a topical drug delivery approach that utilises ultrasound as a physical stimulus to enhance permeation of active pharmaceutical ingredients through the skin. Only limited research has however been conducted to evaluate the potential of ultrasound-responsive drug carriers, such as gas microbubbles, in sonophoresis. Franz diffusion cells have been extensively used for measuring drug permeation in vitro; however, traditional systems lack compatibility with ultrasound and only limited characterisation of their acoustical behaviour has been carried out in previous research. To overcome this limitation, we designed and manufactured a novel Franz cell donor compartment coupled with a V-shape PDMS lid and a conventional glass receptor, and performed a functional characterisation of the assembly for application in sonophoresis with ultrasound-responsive microbubbles.

Methods:
The US-compatible Franz cell donors were conducted using an online 3D model design program. 3D-printing was used for fabricating the donors with the transparent resin. Comparative studies between glass and 3D-printed Franz cell donors were conducted including sealing performance and imiquimod absorption. Ultrasound at an excitation frequency of 1.1MHz was employed to measure the acoustic characteristics of 3D-printed donors. The preparation and characterization of imiquimod-loaded microbubbles were conducted to establish a US-mediated drug delivery system. Consequently, in vitro permeation studies utilizing Strat-M membrane were conducted to evaluate the differences between this novel system and traditional system, as well as to explore the enhancement of drug permeation facilitated by US-mediated microbubbles.

Results:
The assembly was capable of effectively retaining liquids during prolonged incubation and the absorption of imiquimod onto the 3D-printed material was comparable to the one of glass. Moreover, a predictable ultrasound field could be generated at a target surface without any significant spatial distortion. Finally, we demonstrated applicability of the developed assembly in sonophoresis experiments with StratM®, wherein ultrasound stimulation in the presence of microbubbles resulted in significantly enhanced drug permeation through and partitioning within the membrane (2.97 ± 0.35 µg and 3.91 ± 0.41 µg) compared to passive diffusion alone (1.74 ± 0.29 µg and 2.29 ± 0.32 µg), over 24 hours.

Conclusion:
A new Franz cell donor compartment was designed and fabricated using 3D printing, and was then coupled with a PDMS lid and a conventional glass receptor to generate an ultrasound-integrated Franz cell assembly. The system was characterised for its physical performance and feasibility for use in drug permeation studies involving US-responsive microbubbles. In addition, to address the tendency of microbubbles to float upwards, the newly developed Franz diffusion cell system can be inverted for five minutes. This ensures that the microbubbles remain securely attached to the membrane during ultrasound treatment.

P24. The study of interaction between the skin barrier lipids and the corticosteroids through model systems

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The human epidermis consists of keratinocytes arranged in different layers, with the key layer being the outermost stratum corneum (SC), where the skin barrier is localized. The SC is composed of the corneocytes, dead keratinized cells, surrounded by very organized lipid matrix. The lipid matrix comprises ceramides (Cer), free fatty acids (FFA) and cholesterol (Chol) in equimolar ratio, and its composition and arrangement, are essential to maintain epidermal homeostasis. Any changes in lamellar and lateral organization and composition of the SC lipids can lead into inflammation, associated with various skin diseases. In general, topical medications based on anti-inflammatory drugs like corticosteroids are the most common used to treat mild to moderate psoriasis and atopic dermatitis, however they have multiple side-effects and how their effect on the skin barrier lipids is not well known.
The aim of this study was to evaluate the effect of topically applied anti-inflammatory drug on the microstructure of skin barrier models. We investigated the interactions of three different corticosteroids (Hydrocortisone butyrate, Betamethasone dipropionate and Clobetasol propionate) with the skin barrier lipids. We prepared a simple artificial model membranes containing isolated extracted human barrier lipids (250 μg/cm2), with the addition of one of the corticosteroids in five different concentrations according to their clinical doses. To better understand the biophysical behavior of the barrier lipids with the drug we studied the changes lamellar and lateral organization. The lateral packing (presence of orthorhombic/hexagonal/fluid arrangement) and lipid chain order were studied by Fourier Transform Infrared (FTIR) Spectroscopy. The relative orthorhombic phase content in all the studied model mixtures was calculated. The lamellar organization (the presence and values of the long periodicity phase) was assessed by X-ray diffraction.
These results can help better understand the skin barrier (patho)physiology, how the corticosteroids interact with the skin barrier and support similar investigations, providing valuable insights for the design of topical formulations with anti-inflammatory drugs for the treatment of skin diseases.
We would like to acknowledge the Czech Science Foundation (25-17203S) and Charles University (SVV 260661, GAUK 432825). Additionally, we would like to recognize the contribution of student Parsa Paydar.

P25. Accounting for epidermal turnover and binding in dermal absorption predictions

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Accurately quantifying dermal absorption is critical for safety in regulatory risk assessments. Traditional studies using excised skin may overestimate systemic absorption, as they rarely account for epidermal turnover and desquamation, given the skin is often non-viable. These processes can reduce the bioavailability of dermally absorbed compounds, as material may be lost along with desquamated cells. With increasing efforts to reduce animal studies and the limited availability of human in vivo data, in silico models have become valuable in dermal absorption research. While a few in silico models have included epidermal turnover,[1-3] they lack comparison with experimental data. The aim of this work is to improve dermal absorption values for risk assessments by incorporating the impact of epidermal turnover through computational modelling. The developed model will be validated by comparison to experimental data, providing a more comprehensive assessment of the impact of turnover.

An in silico model is being developed based on the equations by Reddy et al.,[1] who introduced a convective term to Fick's second law to account for epidermal turnover. Initial findings suggest systemic absorption differs significantly when turnover is included for heavier, lipophilic compounds, while smaller, fast-permeating compounds show minimal differences. Experimental data indicates that the model does not fully capture skin retention when using only Log P and molecular weight for selected compounds. A key area for further exploration is the modelling of keratin binding in the stratum corneum, as compounds bound to keratin are immobilised, either temporarily or permanently, but can still be removed by turnover. New binding data will be collected, capturing both fast reversible binding and slower or irreversible binding processes under conditions more representative of the stratum corneum than the current literature. With the addition of new binding data to better model retention and removal of compounds, this work is expected to provide valuable insights into the effect of epidermal turnover relative to diffusion and binding processes—an aspect that has not been fully addressed in currently published models. Ultimately, it will contribute to more accurate dermal absorption predictions for risk assessments.

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P26. Establishment of a RHE Inflammation Model in vitro and Analysis of Scutellaria Baicalensis, Soy and Germ Extract

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Introduction: Animal studies are used to test product safety before human trials. Their predictive value is limited due to morphological skin differences and should be avoided for both standardization and ethical reasons in cosmetics and medical products. 3D alternative in vitro is reconstructed human epidermis (RHE) with multilayered human keratinocytes and a Stratum Corneum barrier. Thus, RHE is histologically like human epidermis in vivo[1]. RHE models are used to study inflammatory responses[1,2]. Our study focused on the establishment of a RHE inflammation model to evaluate the anti-inflammatory properties of Baicapil™, an active complex of three extract mixtures of Scutellaria Baicalensis Root, Glycine Soja Germ and Triticum Vulgare Germ[3]. It promotes hair growth, when applied topically.
Material and Methodes: In our experiments, RHE models were equilibrated overnight and then first treated for 24 h with various compounds, such as Sodium Dodecyl Sulfate (SDS) or Lipopolysaccharides (LPS), SkinEthic™ maintenance medium (SMM) or Dulbecco's phosphate buffered saline as negative controls. We used hydrocortisone (HC) at 150 µM as positive control. Formulations tested were Baicapil™ and Baicapil™ placebo. After first treatment and 20-fold washings, RHE models were treated afterwards with SDS or SMM for further 24 h. The supernatants were collected and tumor necrosis factor α (TNFα) and Interleukin-1α (IL-1α) were determined by Enzyme-linked Immunosorbent Assay.
Results: We found that TNFα concentration in the medium was higher after SDS than after LPS treatment, while SMM was a suitable negative control. Pre-treatment with Baicapil™ resulted in lower TNFα and IL-1α levels than incubation with SDS alone. These levels were comparable to post-treatment with SMM instead of SDS. TNFα and IL-1α levels in the medium of the samples pre-treated with HC were also within this range. Consequently, treatment with Scutellaria Baicalensis, soy and germ extract showed a similar behavior to treatment with HC.
Conclusion: The establishment of a method to study the benefit in RHE models was successful. Baicapil™ shows a tendency to lower TNFα and IL-1α levels compared to SDS, similar to HC, indicating anti-inflammatory properties.

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P27. In vivo Evaluation of Prototype for Quantitative Skin Surface Temperature Recording

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Introduction: In medicine cooling thermal burns with running water is a recommended first aid intervention. Hydrogels for treating superficial cutaneous wounds were demonstrated to effect an intermediate cooling. A standardized procedure for recording skin surface temperature changes with respect to differing procedures, varying composition and dosage will enable to quantify the cooling capabilities of topical products. Having developed and evaluated our skin surface temperature prototype in vitro, we used the safe and ethically acceptable device to quantify cooling effects in real time in vivo. In the present proof of concept study, the skin temperature following application of 1) pre-cooled water and 2) a cooling gel were measured. From the course of the curves the maximum temperature difference to the baseline (ΔTmax) and the area under the cooling curve (AUC) were computed. In additional experiments, 3) in situ and in vivo water heating was recorded. Material and Methods: Left forearm inside, 5 cm distant from elbow served as an easily accessible measuring field. Distance of the sensor from the surface was 15 mm with a field of view of 35°. 1) Following a 5 min settling phase, 10 mL of water pre-cooled to 6°C (temperature from refrigerator) or to 15°C (representative value for tap-water) was applied for 1 min and quickly removed. Then the skin surface temperature was recorded for 20 min to investigate the cooling effect. 2) A representative cooling gel (BepanGel® Wundgel) was topically applied at different doses from 0.98 to 14.9 mg gel per cm² skin. Results: 1) For pre-cooled water, a fast and pronounced surface temperature shift was followed by a saturating exponential. Water pre-cooled to 15°C (n = 4) and 6°C (n = 5) resulted in ΔTmax of 11.0 ± 0.7 K and 15.7 ± 0.2 K, respectively. The AUC changed from 21 ± 2 min·K (15°C) to 33 ± 4 min·K (6°C). 2) For the cooling gel, the surface temperature decreased quickly by 2-4 K to remain constant for up to 7 min, before it returned to baseline following a saturating exponential. The AUC for the highest dose was greater than for water pre-cooled to 6°C. Rank correlation analysis showed a negative relationship between ΔTmax and the mass of gel applied (RΔTmax = 0.89; n = 16). Regression through the origin showed a negative linear relationship between AUC and mass of gel (R2adj = 0.97; n = 16). 3) In situ and in vivo heating of water could be well-described by a model for heat conduction in a plane sheet. Summary and Outlook: Our prototype has successfully demonstrated its use in relevant in vivo applications and will be used to study the impact of the body region and other topically applied vehicles or finished products.

P28. Dosimetry of Limonene as Volatile Organic Chemical in Gas Phase Exposure System for Topical Dosing

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Introduction: A transparency list of the International Fragrance Association includes approximately 2,700 saturated and unsaturated chemicals with different functionalities. Next to scenting properties, fragrances also partly exhibit anti-microbial, anti-inflammatory and skin penetration enhancement activities and are therefore of interest in medical application. Common to all fragrances is a low molecular weight, a low boiling point (BP), but a broad range in lipophilicity (e.g., 2,3-Heptanedione with Log P 0.14 to Olive oil with Log P 23.08). Increasing Log P correlates directly with the aqueous solubilities. To emphasize this fact, 50% of the fragrances exhibit a Log P > 3.5 and are considered as "challenging chemicals" in non-animal New Approach Methods (NAMs) according to 3R. These chemicals do not dissolve in water or cell culture media and are categorized as "not testable". Further challenges are based on the fragrance volatility. A constant dosimetry is difficult to control, this leads to a possible false-negative evaluation of the fragrance in vitro or to a cross contamination and thus false-positive evaluation in controls and other fragrances in parallel experiments in risk assessment. Fragrances can also oxidize abiotically and form secondary structures. Dosimetry of limonene in a Gas Phase Exposure System is a suitable lead structure due to its lipophilicity (Log P 4.83) and its oxidability to establish a controlled topical dosing. Material and Methods: A 12/6 in vitro Gas Phase Exposure System (Vitrocell Systems GmbH, Waldkirch, Germany) with a peristaltic pump to deliver, a heating line to evaporate limonene and an isokinetic dilution with compressed air and distribution to six parallel cell culture inserts was installed. After the heating line and isokinetic dilution, sampling points (SP) 1 and 2 are obtained with three in series connected trapping units filled with acetonitrile. SP3 was filled with 0.5 mL DMSO as surrogate for in vitro cell cultures. Limonene and selected oxidation products were purchased from Merck (Darmstadt, Germany). Results: A combination of 2.5 mL compressed air and peristaltic pump flow of 0.8 mL limonene per min achieved most constant aerosol for subsequent evaporation in the heating line. For 4 hours, mass transport at SP 1-2 reached a plateau at approx. 40 mg limonene/min. At SP3, limonene concentration was nearly constant in dosimetry pots with 4.54 µg ± 1.64 µg (n=18) at 15, 60 and 240 min. No oxidation products were detected.
Summary and Outlook: Using the example of limonene, a Gas Phase Exposure System is fundamentally suitable for creating a solvent-free and controlled topical exposure. Further characterization of the dosimetry will include fragrances with higher BP and varying Log P.

P29. Unveiling the 3D texture of topical semi-solid formulations using micro X-ray computed tomography. The example of bigels

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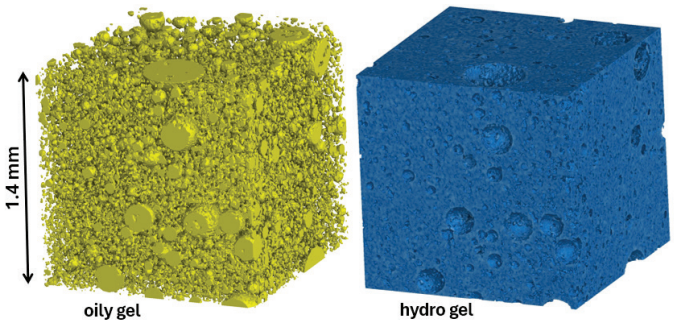
It is well established that the microstructure of topical semi-solid formulations can strongly influence their properties, both in terms of active delivery and sensory perception. These formulations offer many advantages over solid formulations, for example allowing local as well as systemic delivery or strengthening consumer adherence. On the other hand, their preparation is delicate: the use of matrix materials, such as oils, water, water-soluble polymers, or alcohols leads to micro-structured materials whose structure is highly process-dependent and stability is sometimes reduced, affecting the release rate and bioavailability.

The tools for characterizing this microstructure at the disposal of the formulator are not well suited to semi-solid forms because of their fluid nature. For instance, optical microscopy can only provide images of products crushed between slide and coverslip. This limitation can be overcome using an emerging 3D imaging technique, X-ray microtomography. This radiography technique allows us to visualize, digitize and analyze quantitatively the interior of a product without any sample preparation. When coupled to X-ray beams produced by a synchrotron facility, the performances of this technique (µ-XCT) perfectly match the requirements to visualize in 3D semi-solid formulations: micrometer spatial resolution with enough contrast to distinguish aqueous phases from oily phases (without any staining).

To illustrate the potential of the µ-XCT technique, observations were made on a bigel stabilized with the ready-to-use oil stabilizing agent Emulfree® Duo. Bigels are hybrid dispersions of an oily gel network within an aqueous gel, offering versatile properties derived from both gel types. The comparison of the microstructures of the bigel and of the emulsion in which Emulfree® Duo has been replaced by classical O/W emulsifier is striking. The 3D reconstructed volumes of the bigel obtained with a pixel size 0.7x0.7 µm2 and high contrast density (phase contrast mode acquisition) mainly shows low-density globules (10-250 µm diameter) dispersed in the denser continuous phase whilst the classical emulsion microstructure consists of a moderately dense phase in which less dense small globules (a few µm) are dispersed. This specific bigel microstructure is probably related to the pleasant sensory feel, to its excellent stability and to its good spreadability that are measured by other sensory and rheological analyses.

The combination of micro-morphological information and macroscopic data is a powerful tool for the rational development of formulations by linking 3D microstructure, chemical composition and feedback from consumers.



Pseudo-3D images of oily (yellow) and hydro (blue) gels in a small volume of bigel Emulfree® Duo after virtual separation of µ-XCT reconstructed volumes.

P30. DEVELOPMENT OF LIPID NANOCAPSULES FOR DERMAL DELIVERY OF JAK INHIBITORS

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Representatives of Janus kinase inhibitors are immunomodulators approved for the treatment of severe skin diseases such as vitiligo or atopic dermatitis. Nowadays, their potential effect on skin cancer treatment is also very deeply investigated. However, the extensive use of Janus kinase inhibitors in clinical practice is limited by low bioavailability into the skin tissue after systematic administration, resulting in serious side effects. One way to overcome these limitations is the application of different types of nanoparticles. This study is aimed at investigating the effects of various nanoparticulate formulations on the ability of permeation of a selected JAK inhibitor (JAKI) into and through the skin. First, an extensive solubility study of JAKI was conducted. The solubilities were determined in the commonly used excipients in dermal dosage forms (e.g. MCT oils, Tween 80, propylene glycol). With regards to this solubility study, the appropriate nanoparticulate formulation based on lipids called lipid nanocapsules (LNC) was designed. The LNC was prepared by temperature phase inversion and characterized by DLS (size, polydispersity index), and a pilot stability study was performed at 4°C and 25°C. The lead LNC formulation was chosen according to the long-term stability and encapsulation efficiency of JAKI. JAKI was successfully incorporated into LNC with high encapsulation efficiency. The stability of LNC nanoformulation reached 1 month. Finally, the effectivity of LNC formulation was proved in ex vivo studies on porcine skin over 48 hours. This study proved the efficacy of our LNC formulations against the simple JAKI suspension in 60% propylene glycol used as a standardized control for this type of study.

P31. A Regulatory Framework for Bioequivalence Assessment of Topical Drugs

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Topical semisolid formulations are classified as complex systems due to their microstructure. As such, when developing a topical generic drug product, it is of paramount importance to scientifically and regulatory substantiate its equivalence towards the reference product, in all characteristics inherent to their microstructure, performance and efficacy. However, achieving so may be challenging, due to semisolid pharmaceutical complexity, but mainly due to the practical/operational and statistical constraints related with the documentation therapeutic profile equivalence, which is mainly supported by in vivo methods, as well as by in vitro permeation testing. In fact, due to these hurdles regulatory agencies like European Medicines Agency (EMA) and the Food and Drug Administration (FDA) actively seek the development of surrogate methodologies, able to consubstantiate efficacy equivalence demonstration.
In light of the above, this work aims to develop a framework capable to assess the efficacy profiles of these products, by exploring promising alternative methods for demonstrating bioequivalence (BE) of topical generic product for topical application. Specifically, alternative methodologies such as photoacoustic tomography and disease models are addressed to assess the drug permeation through a three-dimensional (3D) bioprinting synthetic skin and the drug therapeutic behaviour in its pathophysiology scenario, respectively.
These methods intend to document BE through more robust and efficient methodologies, while reaching the same quality as the currently accepted strategies – in vitro permeation testing, tape stripping, vasoconstrictor assay and clinical endpoint studies. These surrogate methods will lend more credibility to generic manufacturers, besides supporting new possibilities for scientific breakthroughs in the topical drug delivery field.

P32. In vitro release test development for arbutin-loaded chitosan/hyaluronic acid polyelectrolyte complex films for cosmetic use

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This study investigated the release rate of arbutin, a natural skin-brightening agent, from chitosan/hyaluronic acid polyelectrolyte complex films for cosmetic use. The influence of plasticizer (glycerol) and crosslinkers (sodium citrate and tannic acid) on arbutin release as well as the volume of the medium and the type of dissolution apparatus were investigated. To prepare films, equal amounts of chitosan (1% w/w) and hyaluronic acid (0.5% w/w) solutions with or without the addition of plasticizer/crosslinker (20% of the polymer mass) were mixed and then arbutin (15% of the polymer mass) was added. The mixtures were poured into silicone molds and air-dried for 96 h. Arbutin release from films (3 cm x 3 cm) containing 3 mg of arbutin and attached on disks with 41.2 mm diameter, was tested in phosphate buffer saline pH 5.5, at 32 ± 0.5 °C and agitation speed 50 rpm. For 100 ml of medium, a shaking water bath LSB18 Aqua Pro (Grant, UK) was used, while for 150 ml and 200 ml experiments were performed on rotating mini paddle apparatus (DT 126 light, Erweka, Germany). Arbutin quantification was performed spectrophotometrically at 280 nm (Evolution 300, Thermo Scientific, USA). When 200 ml of medium was used, most absorbance values were below the limit of quantification, preventing a reliable determination of arbutin release. In 100 ml and 150 ml of media, all formulations showed an immediate release profile, with complete arbutin release within the first 15 min. The type of dissolution apparatus and media volumes (100 ml or 150 ml) did not significantly affect the release, suggesting that hydrodynamic factors do not alter the release behavior of arbutin as highly water-soluble substance. Further comparisons of arbutin release were performed in 150 ml medium with mini paddle over disk assembly. The greatest differences in arbutin release were formulation-dependent. Films without plasticizer/crosslinkers achieved complete arbutin release the fastest (104.56 ± 1.52% after 10 min), while other formulations achieved complete release within 15 min (99.69 ± 4.77% from films with glycerol, 100.49 ± 3.15% from films with tannic acid, and 103.25 ± 1.21% from films with sodium citrate). Plasticizer and crosslinkers caused a moderate reduction in the arbutin release rate, but did not alter the immediate release properties of films. Based on these results, these films can be recommended for fast-acting treatments, e.g. for a 10-30 min application before their removal from the skin.

P33. Cryo Emulsiongel Patches: Influence of the Oil Type on Emulsion Stability and Dermal Drug Delivery

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Emulsiongels are receiving increasing interest as an innovative vehicle for drug delivery by combining the properties of conventional emulsions and hydrogels. This provides a synergistic effect through the ability to transport lipophilic drugs as well as additional physical stabilisation of the thermodynamically unstable emulsion by an outer gel matrix. The additional cross-linking of the gel phase provides the decisive advantage of a patch for long-term application. Poly(vinyl alcohol) (PVA), as a polymeric emulsifier and gelling agent capable of physical cross-linking by cryogelation [1], is an excellent dual player in the development of such a skin-friendly and non-irritating vehicle.
The present study investigates the suitability of different oil types for emulsiongel formation by cryogelation and thus the use of sub-zero temperatures, which are known to have a negative effect on the emulsion stability. The effect of the incorporated oil phases on drug release and transdermal transport was also investigated.
Oil-in-water emulsions were prepared with different types of oils, an aqueous solution of PVA 8-88 as emulsifier and subsequently combined with the aqueous solution of PVA 56-98 as a gelling agent. The emulsions were then subjected to cryogelation for physical cross-linking using conditions optimised in previous studies [2]. Lidocaine was used as a lipophilic drug.
The used oils and emulsions were characterised by differential scanning calorimetry. In vitro release and permeation studies were carried out on selected emulsiongel patches using Franz diffusion cells. To verify the stability of the emulsions after cryogelation, the droplet sizes were analysed by Raman spectroscopy within the patches as well as by laser diffractometry after thermal de-crosslinking.
The results show different suitability of oils for cryogelation, with medium chain triglycerides, castor oil and rapeseed oil performing best. Consequently, emulsions containing them were further characterised and showed no considerable increase in droplet size. Controlled drug release was verified over a period of 48 hours, with release and permeation rates varying according to the oil used. In conclusion, it is possible to incorporate selected oils into a cryogel matrix without loss of emulsion integrity. Thereby, an innovative vehicle for the delivery of lipophilic drugs may be developed.

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P34. Nanoparticulate systems for topical delivery of Itraconazole

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Fungal skin diseases are highly prevalent, affecting nearly a billion people worldwide. Despite the availability of various oral and topical antifungal formulations, poor bioavailability, drug interactions, low skin permeability, adverse effects, and frequent application needs lead to insufficient treatment efficacy and patient discomfort. For topical formulations, achieving adequate drug concentration at infection sites remains challenging due to the poor aqueous solubility, large molecular size, and high lipophilicity of antifungal drugs like itraconazole (ITZ). To address these challenges, nanoparticulate systems offer significant promise in enhancing bioavailability, efficacy, stability, and targeted delivery to specific skin regions and follicles. In this study, we developed three different nanoemulsions, polymeric nanoparticles, and nanocrystals for the topical delivery of itraconazole. All developed ITZ-loaded nanoparticulate systems were characterized using dynamic light scattering (DLS) to assess particle size, distribution, and surface charge, as well as scanning electron microscopy (SEM) to evaluate surface morphology. The aim of this study was to identify the most efficient system that can overcome skin barriers and address the physicochemical challenges of ITZ, ultimately improving its skin bioavailability. To evaluate the most efficient system, ex vivo skin permeation was conducted using Franz diffusion cell systems with porcine skin. In addition, drug distribution in the epidermis and dermis was assessed using ex vivo skin separation studies. The results revealed that ITZ nanocrystals exhibited superior efficiency compared to the other developed systems, with the highest dermal entrapment of ITZ. In vitro release studies were then performed with the ITZ nanocrystals to assess their release behavior, and different dialysis devices (e.g., SnakeSkin™ Dialysis Tubing, Falcon tubes, etc.) were compared to identify the most suitable one based on the release profiles. In conclusion, the nanocrystals hold significant promise in overcoming the troublesome physicochemical properties of ITZ, highlighting their potential for effective topical delivery.

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P35. Cutaneous and Follicular Delivery of Bioactives from Natural Plant Extracts using Nanoemulsions: A Case Study using Rice Bran Oil

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Rice bran oil (RBO), a by-product of rice milling, contains bioactive compounds (BCs) with antioxidant properties. However, the oil is difficult to incorporate into aqueous formulations and the low individual concentrations of key BCs limit its utility for topical application. This study aimed to develop an optimized RBO-based nanoemulsion (NE) to enhance cutaneous delivery of three key BCs in RBO: 24-methylene cycloartenol ferulate (24-MCF), γ-tocotrienol, and β-sitosterol. Pseudo-ternary phase diagrams (10% RBO, 5% surfactant mix, 85% ultrapure water) and ultrasonication (40% amplitude, 60 s) were used to prepare the NE, resulting in small globules with a diameter of 222 nm and a PDI of 0.287. A conventional emulsion (EM) with the same composition was also prepared (but without ultrasonication) for comparison – these droplets had significantly larger size (1678 nm) and displayed greater variability (PDI 1). An RBO dispersion in hydroxypropyl methylcellulose (HPMC) served as the control. The cutaneous biodistribution of the BCs was evaluated using porcine skin mounted in vertical Franz diffusion cells for 8 hours under infinite dose conditions (25 mg/cm² of RBO). An innovative punch biopsy method was used to evaluate follicular delivery by comparing PSU- and non-PSU-containing skin samples [(1)]. Quantification was done using a validated UHPLC-MS/MS bioanalytical method. The NE exhibited excellent physical stability over a period of three months at 4°C. Cutaneous administration of NE resulted in skin deposition of 4.14 ± 0.85, 2.94 ± 0.35, and 3.75 ± 0.63 nmol/cm² for 24-MCF, γ-tocotrienol, and β-sitosterol, respectively. These values were significantly higher than the control formulation (0.72 ± 0.42, 1.4 ± 0.33, and 1.3 ± 0.55 nmol/cm² for 24-MCF, γ-tocotrienol, and β-sitosterol, respectively). The cutaneous biodistribution profile revealed preferential accumulation in the stratum corneum and epidermis. Although NE and EM resulted in similar cutaneous deposition of the BCs, the NE significantly enhanced follicular delivery, which was ~2-fold higher in PSU-containing samples as compared to control samples. No such difference was observed with the EM. It is likely that the smaller globule size of NE played a crucial role in facilitating follicular delivery, which may be a means to enhance cutaneous bioavailability of BCs. The results show the potential of RBO-based NE as a promising approach for the targeted topical delivery of its antioxidants.

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P36. Enhancing formulation substantivity using silicone resins

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Silicone compounds have been used for years in the pharmaceutical industry for various applications, with topical formulations being the most common one. These compounds have a low surface tension, a high gas permeability and are resistant to oxidation, making them exceptionally stable and immune to microbial contamination. Despite their advantageous characteristics, silicones have faced growing criticism due to their non-biodegradability and environmental persistence [1]. While eliminating their use entirely is one approach, another option is to mitigate their environmental impact by reducing the application frequency. Substantivity, the ability of a formulation to adhere to the skin and resist removal through contact with other surfaces, plays a crucial role in this context. A highly substantive formulation not only minimizes environmental loss but also reduces the frequency of application by ensuring more of the active pharmaceutical ingredient (API) remains on the skin, improving penetration and permeation [2]. A broad range of silicones is used in topical pharmaceutical formulations. One of these are resinous siloxanes, which are polysiloxanes with a highly cross-linked network. In addition to other properties, they also have film-forming characteristics [1]. Since silicone compounds are neither water-soluble nor miscible with fatty oils or paraffin oils, they present an interesting option in formulating two phased systems [3]. This study presents the results of formulating such film-forming silicone resins in an oil-in-oil emulsion to enhance substantivity.
Various oil-in-oil emulsions containing avobenzone as a model API were developed. The outer phase comprised a silicone oil with an incorporated film-forming silicone resin, while the inner phase consisted of a lipid phase, such as castor oil. Different silicone emulsifiers were used as stabilizers. To characterize these formulations, substantivity was assessed using an in-house developed method [2], rheological properties and the droplet size were investigated.
Studies indicated that silicone resins exhibit surface activity and adsorb preferentially at the interface, destabilizing the emulsions in the process [4]. Emulsions were thus optimized to account for this effect and ensure storage stability.

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P37. In vitro permeation studies of metronidazole in porcine skin

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Purpose
Rosacea is a chronic condition that includes redness of the face accompanied by pimples and pustules. Metronidazole is a nitroimidazole derivative commonly used to treat rosacea. The development of targeted and effective metronidazole skin preparations is important because long-term oral administration of this drug is associated with tolerance and side effects. The aims of this work are to (i) develop a range of simple systems for metronidazole delivery and (ii) evaluate skin delivery from these systems with Franz cell studies.

Materials and Methods
Porcine ear skin was prepared as 20 mm discs, and used for permeation studies in Franz diffusion cells (32 ± 1°C). For mass balance validation, metronidazole (10 mg/mL in benzyl alcohol) was applied as a 10 µL finite doses to porcine skin. After 4 h, 1 ml of water: methanol (50:50) was used as a solvent to clean the surface. The first wash was carried out 30 times, the second and third wash was conducted 10 times each. Washes from the skin surface, applicators, cotton buds, and skin fragments were analysed using a validated HPLC method. For single solvent permeation, metronidazole solutions were prepared with benzyl alcohol (BA), Transcutol® P (TC), and 1,2-propanediol (PG). The receptor compartment of Franz cells was filled with a defined volume of PBS solution (pH=7.3 ± 0.2) to ensure skin conditions. A dose of 10 µL of solutions was applied to the skin surface. Receptor phase samples were collected at different time points up to 24 h, followed by mass balance studies. All samples were analysed with HPLC.

Results
The mass balance recovery of metronidazole in porcine skin was calculated, and the accuracy of the experimental method was verified. The recovery was 98.13% ± 3.66%. The recovery result is within the acceptable range of 90-110%, as defined by OECD guidelines 2004a and 2004 b, which means the method is reliable. The 24 h cumulative permeation amounts of metronidazole through porcine skin from BA, TC, and PG were determined as 2.32 ± 0.71, 4.91 ± 1.30, and 2.87 ± 0.46 µg/cm², respectively (mean ± SD, n=3). At 24 h, TC exhibited superior permeation (6.07% ± 1.24%) compared with BA (2.28% ± 0.93%) and PG (3.25% ± 0.85%) ($p<0.05$). Similar quantities of metronidazole were extracted from the three solutions for porcine skin ranging from 10.71% - 18.14% ($p>0.05$).

Conclusion
TC increased the porcine skin permeation of metronidazole more effectively than PG and BA. It has been hypothesised that TC partitions into the stratum corneum and saturates the intercellular lipid domain. This would allow greater drug distribution to the stratum corneum. At the same time, TC may easily penetrate the stratum corneum and strongly interact with water in the intercellular pathway to enhance drug penetration. Future studies will investigate more complex solvent systems as well as how these systems behave in vivo.

P38. Bicontinuous cubic mesophases for epicutaneous patch testing of contact allergy

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Patch testing is the gold standard diagnostic tool for detecting allergic contact dermatitis caused by haptens including metals and fragrances1. However, traditional carriers like petrolatum, commonly employed in patch testing, encounter challenges in dissolving hydrophilic allergens such as salts2. This limitation hampers the effectiveness of patch testing procedures. Lyotropic liquid crystalline mesophases offer a promising alternative due to their ability to accommodate both hydrophobic and hydrophilic substances3. In this study, we investigate inverse cubic mesophases formed by glycerol monooleate (GMO), diglycerol monooleate (DGMO), propylene glycol (PG) and water as potential carriers patch testing, starting with nickel allergy.
In vitro release experiments were performed to compare the release of the contact allergen from the lipid-based carriers versus petrolatum. The allergens within petrolatum as vehicle, are stored in prefilled syringes. The personnel apply a specific amount to patient's back. Since several patch tests are performed daily, the formulation must be easy to dispense without requiring high force. Therefore, we have benchmarked our formulations versus petrolatum by determining the force required to handle each vehicle using a texture analyzer. The effects of adding DGMO or PG on structure and rheological properties were evaluated using Small Angle X-ray Diffraction (SAXD) and a Bohlin rheometer.
Release experiments reveal a higher nickel release from lipid-based carriers compared to petrolatum indicating the potential to shorten the application time of the patch on the patient from today's 48h to less than a day. Texture analysis and rheological properties showed that the addition of DGMO or PG leads to lower forced required for handling the formulation.
We hypothesize that bicontinuous cubic mesophases can serve as a universal vehicle for patch testing of a wide range of allergens with varying physicochemical properties. Our future aim is to perform clinical studies where the lipid-matrices will have a dual functionality. This includes evaluating the decrease of patch testing application time and collecting non-invasively endogenous low molecular weight analytes, which could potentially reflect inflammatory skin disorders such as contact dermatitis.

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P39. Effects of fractional laser ablation on gene transcription in viable human skin explants

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Fractional ablative lasers are widely used in clinics for the management of skin conditions, including scars, hyperpigmentation, and wrinkles [1]. The application of optimized laser conditions – e.g. energy, density, and frequency – is obviously recognized as crucial for effective treatment with minimal risk of complications; however, there are few experimental data on the changes induced by fractional ablation at the molecular level in terms of gene expression using human skin [2]. The aim of this study was to investigate the feasibility of using a gene-based approach to quantify expression of key biomarkers in viable human skin explants in response to fractional laser ablation at different energy settings. First, a workflow involving human skin tissue disruption and homogenization, RNA extraction, and Reverse Transcription quantitative Polymerase Chain Reaction (RT-qPCR) was established. Then, this optimized protocol was applied in the subsequent studies – full-thickness human skin explants generated from abdominal surgery were treated with a fractional ablative CO2 laser (UltraPulse ®, Lumenis Be Ltd., Israel) with energy setting of 0 (control), 10, 20, 30 and 40 mJ (n = 3 explants per treatment). Punch biopsies were collected on days 3 and 5 post-treatment, samples harvested on day 0 before treatment were considered as baseline. The biopsies were then subjected to RNA isolation, which was subsequently used in RT-qPCR for six genes associated with fibroblast activation, inflammation, and wound healing: insulin-like growth factor 1 (IGF-1), transforming growth-factor-beta 1 (TGF-β1), interleukin-1 alpha (IL-1α), metalloproteinase 1 (MMP-1), heat shock protein 70 (HSP70), and type I collagen (COL1A1); 36B4 was used as a housekeeping gene to normalize the genes of interest. The preliminary results showed that IGF-1 expression increased with laser energy, peaking at 40 mJ, with a decrease on day 5 possibly due to compromised tissue integrity; while TGF-β1, IL-1α, MMP-1, HSP70, and COL1A1 showed variable trends, reflecting the dynamic processes triggered by fractional laser ablation treatments. Further studies with larger sample sizes are required to validate these preliminary results and to provide insight into the optimal laser conditions in clinical practice and their effects on key proteins in the skin. The preliminary findings obtained so far suggested the potential of the in-house ex vivo human skin model [3] to serve as a robust tool to investigate molecular changes following various treatments.

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P40. Natural product-based thermotropic liquid crystals for anti-infective skin treatments

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Liquid crystalline (LC) compositions with a thermotropic core, derived from natural products – cholesteryl esters and mono-/bicyclic terpenoids, were developed as novel materials for skin drug delivery. These systems were subsequently characterized for their mesomorphic and optical behavior. A key feature of these LCs is their temperature-responsive drug release, triggered by a transition from the crystalline to the liquid-crystalline state at skin temperature.
The influence of terpenoids as chiral dopants on the helical structure of the LCs was investigated, revealing their intrinsic untwisting effect. Fluorescence probe studies demonstrated that cholesteryl esters and terpenoids, as essential LC components, collectively disrupt the tightly packed phospholipid bilayer, thereby facilitating drug penetration. In vitro and ex vivo permeation assays using artificial membranes and full-thickness human skin confirmed that LCs enhance the transdermal delivery of model drugs. Moreover, the release of the drug from the LC formulation is accompanied by a distinct colour change of the material, induced by its interaction with the skin surface.
The application of LC systems was extended to the directed delivery of anti-tubercular compounds. The objective was to treat cutaneous manifestations of tuberculosis by ensuring localized drug accumulation in the dermis, where the pathogens predominantly reside. Ex vivo studies using Franz cell assays on human skin, followed by HPLC analysis, demonstrated dose-dependent extended release of these compounds. Cryostat skin cross-sections revealed that anti-tubercular compounds penetrated all skin layers, with maximum accumulation in the dermis. These findings establish LCs as a promising soft material for targeted dermal delivery of anti-infective agents.
To improve patient compliance, polymer-dispersed liquid crystal films were developed as a dosage form for skin drug delivery. In this approach, LC systems doped with anti-infective compounds were embedded in polymeric matrices composed of natural biopolymers, such as sodium alginate and hyaluronic acid. The anisotropic and temperature-responsive properties of LCs were retained within the polymeric matrix, as demonstrated by the autonomous colour changes of the material at skin temperature.

P41. Effects of styrene oligomers on stratum corneum lipid model membrane

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The widespread distribution of microplastics and nanoplastics, which are generated during plastic production, degradation, and decomposition processes, has hugely impacted human health. Any alterations in the skin's lipid composition, particularly in the stratum corneum (SC), cause a disturbed barrier function and are linked with skin diseases. Additionally, SC is in close contact with the environment, personal care, and cosmetic products, leading to constant plastic exposure. This work aimed to examine the effects of selected plastic-related molecules on skin lipid barrier function. More specifically, the effects of styrene oligomers (styrene dimer and styrene trimer) on the SC lipid nanostructure and the permeability through SC lipid model membranes were investigated. First, the SC lipids were isolated from human skin, purified and characterized. Second, the styrene oligomers were incorporated into the SC lipid model membranes, and their microstructure was studied using X-ray diffraction and Raman spectroscopy. Finally, the alterations to the barrier properties of the model membranes containing the styrene oligomers were compared to control membranes using water and indomethacin as permeants. The X-ray diffraction results of control lipid model membranes showed the reflections of the long periodicity phase (LPP) and cholesterol. The model membranes containing styrene oligomers showed the presence of additional reflections and samples containing styrene trimer showed a statistically significant increase in LPP length, indicating the influence of oligomers on the SC lipid lamellar organization. Raman Spectroscopy indicated a uniform distribution of styrene trimer with minor differences in intensity in the sprayed lipid model membranes. Furthermore, styrene trimer showed its influence on water and indomethacin permeability on SC lipid model membranes. Overall, our preliminary results show that the styrene oligomers influence the microstructure and the barrier properties of SC lipid model membranes; however, further research is required to fully understand the impact of plastic pollutants on skin disease prevalence and prevention.

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P42. Improving Photodynamic Skin Cancer Therapy by Increased Oxygenation

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The aim of this project is to increase the efficacy of photodynamic therapy (PDT) of skin cancer. PDT employs a combination of light energy and photosensitizing agents to treat keratinocyte carcinomas, especially basal cell carcinoma. In skin cancer treatment, PDT mostly relies on the generation of singlet oxygen and downstream reactive oxygen species (ROS), via excitation of the well-known photosensitizer protoporphyrin IX (PpIX). To achieve successful clinical PDT protocols, the development of reliable and realistic in vitro methods that allow for easy and flexible screening and optimization is crucial. The in vitro methodology employed here is a new skin tissue phantom based on the simple two-component system of water and monoolein. In the aqueous dermal environment, this lyotropic system forms a stable inverted liquid crystalline cubic phase that can be utilized to incorporate PpIX and thereby mimic PDT conditions. The tissue phantom's molecular organization are evaluated by SWAXS. With this novel set-up, we have investigated how parameters, such as concentration of the photosensitizing agent PpIX and degree of tissue oxygenation, influence the kinetics of ROS generation. Considering the highly reactive nature and transient existence of ROS, it is difficult to directly quantify their amount. Instead, we utilize the Skin Covered Oxygen Electrode (SCOE) [1] to probe the consumption of molecular oxygen, which is the main source of ROS and thus indirectly reflects the ROS generation. In addition, we explore the possibility of using a combined approach of adding hydrogen peroxide to increase skin tissue oxygenation via native epidermal catalase, which converts hydrogen peroxide into oxygen [2]. This has also been validated using a human epidermoid cancer cell line treated with PDT with different hydrogen peroxide concentrations and light intensities and combinations thereof.

The main conclusions from our preliminary results are:

- PpIX can successfully be incorporated in liquid crystalline cubic phases of water and monoolein, enabling a realistic skin tissue phantom for PDT studies in vitro.
- The developed in vitro setup can probe the oxygen depletion caused by the presence of PpIX in the tissue phantom under photo illumination.
- Addition of H2O2 increases oxygen levels due to native epidermal catalase, which potentially can be used to enhance ROS generation and improve PDT efficacy.
- Hydrogen peroxide increases the cytotoxic PDT effect on A431 cells, and the cytotoxic effect depends on the light intensities.

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P43. Solvent-free Development of TPGS nanomicelles for Follicular Delivery of Spironolactone

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Spironolactone is a mineralocorticoid antagonist indicated for hypertension that is being repurposed through its antiandrogenic activity to treat acne vulgaris. Although oral spironolactone treatment has proven effective in clinical studies, a topical formulation for targeted localized therapy of acne would reduce off-site effects. The first objective of the current study was to use a patented cryomilling manufacturing process, which avoids the use of organic solvent [(1)], to prepare a 0.1% spironolactone TPGS-1000 nanomicelle formulation. This was followed by formulation characterization, an evaluation of its stability, and finally by an investigation of its efficiency for follicular delivery. A design of experiments (DoE) approach was employed to identify key parameters involved in the cryomilling procedure and so optimize formulation preparation. However, the predictive performance of the regression model established in the DoE study was compromised by large inherent data variance and overfitting issues. Two "lead" formulations were prepared (differing only in the inclusion of a cryoprotectant, glucose), characterized and tested in vitro using porcine skin and demonstrated preferential delivery of spironolactone to skin samples containing pilosebaceous units (PSUs). Spironolactone deposition in PSU-containing skin was ~5-fold higher than in PSU-free skin (15.6 ± 6.45 vs. 2.81 ± 0.49 ng/mm² for the formulation without glucose, and 11.9 ± 6.03 vs. 1.43 ± 0.90 ng/mm² for the formulation with glucose). The results confirmed that the TPGS nanomicelles enhanced the targeted delivery of spironolactone to PSUs and could potentially enhance efficacy since this is the site where the drug exerts its anti-androgenic effect to regulate sebum production. Interestingly, we observed regional differences in the biotransformation of spironolactone into canrenone, an active metabolite, as amounts in PSU-free skin were significantly higher than in PSU-containing skin (7.61 ± 3.92 vs. 2.82 ± 0.49 ng/mm2 (without glucose) and 4.40 ± 1.25 vs. 1.44 ± 0.90 ng/mm2 (with glucose)). In conclusion, TPGS micelles were able to deliver spironolactone preferentially to PSUs with the potential to form a reservoir and so enable a sustained drug release at the target site for drug action.

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P44. Influence of excipients on tin fluoride (SnF2) uptake in the TR146 model

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The interaction of actives used in oral care products with the oral mucosa is poorly understood. Tin fluoride (SnF2) is commonly used in oral care products, as a source of fluoride and for antibacterial properties of stannous. The aim of this work is to investigate how excipients that are commonly used in oral care products may influence the uptake of this compound in the TR146 buccal epithelial cell model.
TR146 cells were seeded on ThinCert plates (2×10^4 cells/well), optimized for transepithelial electrical resistance (TEER). Once a plateau in the TEER value was achieved, the cells were utilized for 6-hour SnF2 transport studies. SnF2 was dissolved in DMEM and applied to the apical layer of cells for 6 hours. Samples of media were taken from the basal layer to determine any Sn permeation. At the end of the 6-hour study, a mass balance study was conducted to account for the recovery of the total Sn. The following excipients were also selected for study with SnF2: sorbitol, polypropylene glycol (PPG), glycerol, propylene glycol (PG), polyethylene glycol (PEG) 200, and PEG 400. Samples were analysed using inductively coupled plasma mass spectrometry (ICP-MS).
The TEER value of the TR146 cells reached a plateau value of ~241 $\Omega \cdot cm^2$ on days 27–29 prior to the transport study. Permeation assay results indicated no permeation of Sn in the 6-hour study irrespective of the excipient included. However, the amount of Sn taken up by the cell layer was significantly reduced by the excipient that was included with the SnF2 dissolved in DMEM. Glycerol, PEG 200, PEG 400, and sorbitol significantly reduced intracellular Sn levels by 7 – 22 % ($P < 0.05$) compared with the control (no excipient). PEG 200 had the most significant effect, reducing Sn uptake by 22 % ($p < 0.0001$).
This work shows that the choice of excipient used significantly affects the interaction of the actives with the TR146 model. Future work will compare these results with the porcine buccal mucosa model. The long-term goal is selection of excipients that optimise delivery of SnF2 to target sites in the oral mucosa.

P45. Investigation of functional properties and antibacterial activity of chitosan–clay composite films with tetracycline-hydrochloride

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In this study, chitosan-based nanocomposite films were prepared, and their functional properties (mass, thickness and swelling), drug release, and antibacterial activity were investigated. The natural bentonite clay from the Beretnica deposit in the Republic of Serbia (BB) (cation exchange capacity = 120 meq/100 g) was used for the preparation of BB-drug composite from an aqueous solution of antibiotic (pH 3.4, c=1 mg/mL). Tetracycline-hydrochloride (TCl), low molecular weight chitosan, glycerol (as plasticizer), and a 1% acetic acid solution without or with BB-TCl composite were used for the preparation of starting dispersions. The TCl concentration was 0.2% m/m in both starting dispersions, and the films (30 x 30 mm) (designated FTCl and FBBTCl, respectively) were prepared by casting and solvent evaporation. The average mass and thickness (131 mg, i.e., 145 μm) of FBBTCl were increased compared to the parameters of FTCl (93 mg, i.e., 131 μm). The swelling capacity of the films after 24 h (phosphate buffer pH 5.8 at 37 °C) was 131% for FTCl and 330% for FBBTCl. The drug release study in the same medium showed that a complete amount of TCl was released from FTCl after 3 h, while about 25% of TCl was released from FBBTCl after 24 h. The antibacterial activity of the films was tested against Staphylococcus aureus and Pseudomonas aeruginosa using the log-reduction method. The films were incubated with bacteria inoculum for 48 h. Both FTCl and FBBTCl had intense bactericidal activity inhibiting Gram+ bacteria growth by ≥ 7 log10 CFU/ml compared to the control, 100% cellulose film. P. aeruginosa growth was reduced by 3 log10 CFU/mL and ≥ 8 log10 CFU/mL with FTCl and FBBTCl, respectively.
These results indicate the potential of the composite film containing natural bentonite and chitosan for skin application due to its positive effect on functional and antibacterial properties.
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P46. From Aggregation to Activity: Developing a Topical Enzyme Replacement Therapy for a Rare Skin Disease

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This research focuses on the development of a topical enzyme replacement therapy for a rare genetic skin disease. The main objectives include optimizing the recombinant expression, stabilization, and formulation of a therapeutic skin protein. It plays a crucial role as one of the key enzymes in the formation of the cornified cell envelope during the terminal differentiation of keratinocytes in the epidermis. Its malfunction results in an impaired skin barrier, leading to increased transepidermal water loss and the formation of hyperkeratosis. Previous observations have shown that the skin protein tends to aggregate.
To overcome this challenge, various solubility-enhancing fusion tags have been tested that can improve the solubility of proteins which tend to aggregate and form inclusion bodies [1;2]. The characterization of the new fusion proteins was performed by SDS-PAGE and measurements of the specific enzyme activity with a commercially available fluorescence assay specific for this protein family. One of the investigated fusion proteins showed an outstanding increase in enzyme activity due to the solubility tag. Furthermore, various stabilizing additives such as reducing agents and surfactants for the liquid protein formulation were evaluated in stability tests lasting several weeks. By using the reducing agent DTT and the non-ionic surfactant poloxamer 407 as a stabilizer, high stability, measured in terms of activity and protein recovery, was achieved over a period of at least one month.
Overall, the higher activity and good stability of the fusion protein offer encouraging possibilities for the development of a topical enzyme replacement therapy in the form of a hydrogel.

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P47. Potential of two innovative acrylate derivatives for gelation of fragile low-energy nanoemulsions

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Introduction: When developing nanogels, the preservation of nanodroplets within the gel network is crucial for achieving the improved drug delivery. This research closely examined the internal structure of nanoemulsion gels after gelation of a nanoemulsion with two different innovative acrylate derivatives: Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer (SeppinovTM EMT 10) and Polyacrylate Crosspolymer-6 (Sepimax ZenTM).
Materials and Methods: Four different nanoemulsion gels were prepared (NG1-NG4), differing in the gelling agent type and the blank gel-nanoemulsion ratio (1:1 or 2:1). The preservation of nanoemulsion droplets within the 3D gel network was investigated by comparing their droplet size (DLS technique), zeta potential, and pH values before and after transformation to nanogels. The internal structure of nanogels was further investigated using continuous rheology, evaporation rate monitoring, and spreadability testing.
Results: After gelation, all tested nanoemulsion gels preserved the droplet size in the nanoscale (82.09-87.78 nm), but with a wide size distribution (PDI between 0.32-0.40). Higher PDI values can be attributed to the semi-solid nature of the sample, since the non-uniform swelling of the associated polymers can also be detected by DLS as a signal during the measurement. The zeta potential of the nanoemulgels (-35.0 to -42.4 mV) was significantly higher compared to the pure nanoemulsion (-16.6 mV), indicating the formation of new repulsive interactions between the nanodroplets within the gel. pH was found to be in a range of 5.22-5.46 suggesting good compatibility with the skin's pH. Although all samples showed shear thinning behavior, rheology highlighted the differences among internal structure of the tested samples. The nanogels were attributed with maximum apparent viscosities in the following rank order NG2>NG4>NG1>NG3, indicating that more viscous gels were obtained when the blank gel and nanoemulsion were mixed in a 2:1 ratio. Viscosity values correlated well with spreadability results, as the more viscous gels (NG2 and NG4) exhibited less spreading compared to their less viscous counterparts. The evaporation rate was lower for both samples prepared with Polyacrylate Crosspolymer-6, indicating stronger interactions between the 3D gel network and nanoemulsions. Conclusion: Both tested acrylates showed good potential for gelation of nanoemulsions without significantly disrupting the inherent nanodroplet properties. The optimal mixing ratio of blank gels with nanoemulsion was found to be 2:1, since samples NG2 and NG4 showed more rigid internal structure.

P48. Influence of Ethanol as a Preservative in Topical Formulation on the Dermal Penetration Efficacy of Active Compounds in Healthy and Barrier-Disrupted Skin

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Ethanol (EtOH) is a multifunctional excipient often used as a preservative in topical formulations. When added in concentrations above 15% to the water phase, it acts as a natural preservative and is considered to be safe and non-toxic [1]. EtOH is also known to act as a solvent and penetration enhancer and can impair skin barrier function [2]. This study investigated EtOH as a preservative in a commercially available cream (o/w) formulation to evaluate its effect on dermal penetration efficacy [3].

Sodium fluorescein and Nile Red were used as hydrophilic and lipophilic surrogates for active compounds, incorporated at 0.005% (w/w) into creams with and without 20% (v/v) EtOH. Dermal penetration efficacy was assessed using an ex vivo porcine ear model on healthy, intact skin and irritated skin mimicking barrier-disrupted conditions [4]. After topical application, skin biopsies were cryosectioned and analyzed by inverted epifluorescence microscopy followed by digital image analysis [5]. Bio-physical skin properties, including transepidermal water loss (TEWL) and skin hydration were measured to evaluate skin barrier function.

The addition of EtOH to the cream reduced dermal penetration efficacy by 40% for the hydrophilic and 20% for the lipophilic surrogate in intact skin (Fig.1) [3]. In contrast, EtOH had only a minor effect on penetration efficacy in irritated skin. The skin properties were also influenced by EtOH: in intact skin, TEWL increased and skin hydration decreased, indicating dehydrating. In irritated skin, EtOH led to a decrease in TEWL and an increase in skin hydration. These results indicate that skin impairment can be considered to occur in different stages. With further drying, dehydration of the upper skin layers continues and results in a sealing (self-healing) effect. The formation of a thin, dense surface layer – "Pudding skin" – is proposed to prevent further water loss from the skin and to limit dermal penetration of chemicals from the outside.

Differentiating between skin conditions is essential to understand how EtOH, as a preservative, influences topical formulations, particularly in products for sensitive or barrier-disrupted skin. The formation of a "Pudding skin" is proposed as a sealing mechanism that limits water loss and dermal penetration. In summary, the choice and concentration of preservatives and the overall formulation composition are crucial to effectiveness, requiring careful customization to optimize therapeutic outcomes for diverse skin types and conditions.

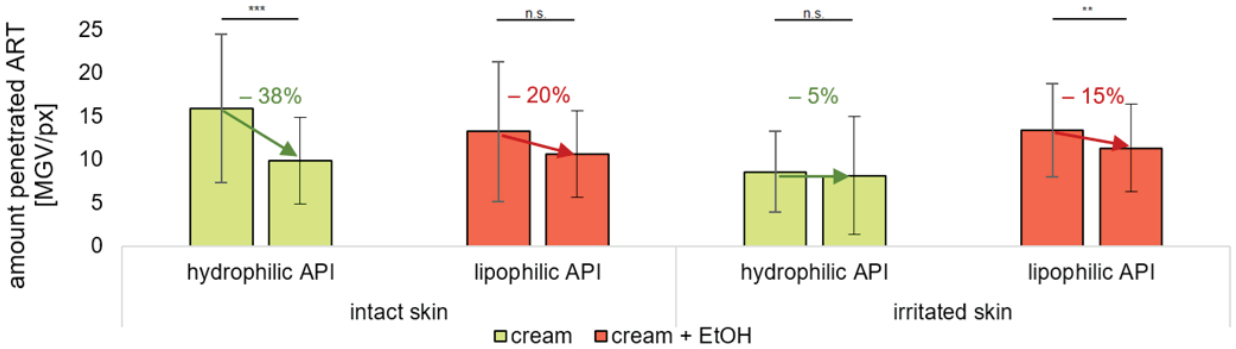

Figure 1: Influence of skin treatment with cream and cream preserved with EtOH (20% v/v) on dermal penetration efficacy of hydrophilic and lipophilic surrogates on intact and irritated skin. n.s. – non significant, ** $\rho < 0.01$, *** $\rho < 0.001$. [3]

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P49. Preformulation and Characterisation of Nifedipine for Topical Drug Delivery Purpose

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Purpose
Nifedipine, a calcium antagonist, was investigated due to its reported efficacy in treating cutaneous lesions caused by peripheral vascular diseases, diabetes, and hypertrophic scars. The specific aims of the research were to characterise the physicochemical properties of nifedipine and to conduct permeation experiments for the development and optimisation of topical nifedipine formulations.

Methodology
An HPLC method was developed and validated to analyse nifedipine. The melting point of nifedipine was determined by Differential Scanning Calorimetry (DSC). The powder form of nifedipine was analysed by X-ray diffraction (XRD). The partition coefficient (Log P) value of nifedipine was measured using the shake flask method. The solvents investigated for solubility and stability studies of nifedipine were dimethyl sulfoxide (DMSO); Transcutol®; dimethyl isosorbide (DMI); polyethylene glycol (PEG) 400; PEG 200; tripropylene glycol (TriPG); methanol (MeOH); 1,2-butanediol; water; isopropyl alcohol (IPA); propylene glycol (PG); 1,5- pentanediol; 1,3-butanediol; isopropyl myristate (IPM), oleic acid. Solubility and stability were also evaluated in a solution of 0.5% BRIJ O20 in PBS solution as a potential receptor phase medium.

Results
The HPLC method for nifedipine was validated according to ICH guidelines. The melting point of nifedipine was determined to be 172.23 °C. XRD analysis confirmed that nifedipine was present as its stable form I. The Log P value was determined as 3.4. Nifedipine showed the highest solubility in DMSO (286.35 mg/ml) with comparatively high solubilities also in Transcutol®, DMI, PEG 200, PEG 400 (123.76, 122.62, 98.69 and 69.53 mg/ml respectively). In contrast, nifedipine was practically insoluble in water (0.014 mg/ml) and slightly soluble in PBS (37.29 µg/mL). Solubility in 0.5% BRIJ O20 was 92.93 µg/mL. Nifedipine was stable over 72 h at 32°C in Transcutol®, DMI, PEG 400, PEG 200, MeOH and 0.5% BRIJ O20 in PBS.

Conclusion
The physicochemical properties of nifedipine were characterised and an analytical HPLC method was successfully validated. The next steps will involve permeation studies in porcine and human skin to identify the best solvents to take forward for development of novel topical formulations of this compound.

P50. Impact of Mutations in Surface-Exposed Residues on the Anodal Iontophoretic Delivery of Negatively Charged Nanobodies

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Constant current iontophoresis enables the non-invasive administration of biologics into and across the skin and is particularly suited for their topical delivery for local therapy of dermatological conditions. It has been successfully used for the (per)cutaneous delivery of cationic proteins – cytochrome C (cyt C), ribonuclease A, human basic fibroblast growth factor and cetuximab. Electrotransport occurs by electromigration (EM), the ordered movement of ions under an electric field, and/or by electroosmosis (EO), the flow of solvent from anode to cathode at physiological pH upon the application of an electric field. Surprisingly, and in contrast to expectations, RNase T1, which is anionic under physiological conditions, was successfully delivered across the skin using cathodal iontophoresis, proving that EM was the dominant transport mechanism (1). Studies with the anti-EGFR 7D12 Nanobody (which is triply negatively charged at physiological pH) and a series of mutants (MW 17.4 – 17.5 kDa) were conducted to better understand the influence of the amino acids present on the protein surface on electrotransport of an anionic protein (2). Mutations were introduced at the surface of the protein to obtain the following mutants: R54E (-5), K65E (-5), S102E (-4) and R54E_S102E (-6). Here, unlike RNase T1, it was found that EO was the governing transport mechanism, meaning the delivery of these proteins was achievable only with anodal iontophoresis. The quantities retrieved in the skin were 6.07 ± 2.11, 9.22 ± 0.80, 14.45 ± 3.45, 11.89 ± 0.87 and 4.28 ± 1.69 µg/cm2 for the WT protein, R54E, K65E, S102E and R54E_S102E, respectively. Their respective cumulative permeation was: 11.39 ± 8.30, 2.94 ± 0.99, 4.18 ± 2.04, 11.63 ± 5.67 and 3.29 ± 3.34 µg/cm2. For the R54E_S102E, both deposition and permeation were low. In this case, the addition of three negative charges led to an increased EM, creating more opposition to EO and thus decreasing the total anodal iontophoretic delivery. These results demonstrate the sensitivity of protein electrotransport to amino acid substitution of only one or two residues. Similar studies are currently being conducted with other mutants: K65E_S102E and E110K.

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P51. Clinical evaluation of skincare products containing turmeric extract: Potential application in managing radiation-induced dermatitis.

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INTRODUCTION: Radiation-induced dermatitis is a common side effect experienced by cancer patients undergoing radiotherapy. Radiation affects cancer cells and normal tissues, leading to skin changes due to free radicals and cytokine activation [1, 2]. Turmeric (Curcuma longa) is an intense yellow pigment spice used for centuries in cooking, cosmetics, dye, and medicinal remedies. Curcumin, the active component of turmeric, exhibits anti-inflammatory, antimicrobial, antioxidant, and anti-neoplastic properties [1, 2, 3]. A large number of studies have been performed on the use of curcumin extract in Radiodermatitis. Due to their equivocal findings, further research is needed [2, 3].
METHODS: The application study of four skincare products containing turmeric extract was conducted on 25 volunteers with a positive history of allergies. The product was tested for skin tolerance using a patch test on healthy adult skin. All tests were conducted in accordance with the guidelines of Cosmetics Europe - The Personal Care Association and Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products.
RESULTS: The results indicated that the tested skincare products were well tolerated by the skin, with no irritation or allergic reactions observed.
CONCLUSIONS: Turmeric extract may offer therapeutic benefits for skin health, when applied topically. Application tests of skincare products containing turmeric extract confirm their usefulness in alleviating radiation-induced dermatitis.
NOTE: Project „Development of innovative dermatological compositions for use during radiotherapy", No. POIR.04.01.02-00-0149/16 co-financed under the Operational Program Intelligent Development 2014-2020, Action 4.1 „Scientific research and development works", Sub-action 4.1.2 „Regional scientific and research agendas"

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P52. Merging SLNs and Ionic Liquids in Semisolid Matrices: Boosting Skin Delivery of Ferulic Acid

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Solid lipid nanoparticles (SLNs) have been widely studied due to their biocompatibility and suitability for skin delivery. However, their low colloidal stability and loading capacity can limit efficiency during storage. Incorporating ionic liquids (ILs) into SLNs and these nanoparticles into semisolid formulations may improve colloidal stability and loading capacity during storage.
This work aimed to develop and characterize SLNs with and without choline-based ILs ([Cho][Gly] and [Cho][Phe]), to load ferulic acid, as model bioactive compound. The incorporation of the SLNs into an Aristoflex® AVC-based gel was also explored. The physicochemical stability of SLNs was followed over time. Their impact on the viability of a HaCaT cell line was also evaluated, as well as the performance in release, permeation, and occlusion assays. The storage stability of the semi-solids was determined over time, in terms of organoleptic properties, pH, and viscosity.
Results showed that both IL-containing nanoparticles were suitable for a topical application, due to their physicochemical properties and colloidal stability. Furthermore, the presence of IL not only seems to contribute to a higher association efficiency and loading capacity, but also modulated the total amount of ferulic acid released, whilst maintaining the occlusive properties of the nanoparticles. The zeta potential of the SLNs was not optimal, thus the incorporation into a semisolid matrix was considered to ensure stability. This incorporation caused a decrease in pH and an enhancement in viscosity, as well as a shift in organoleptic properties from a transparent gel to a white cream, as expected.
This work suggests that IL-SLNs in semisolid matrices can boost the quality of topical formulations for pharmaceutical and cosmetic applications.

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P53. Entoingredients: the future of skin care?

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Sustainability is a key consideration in ingredient selection for topical formulations, aligning with current European Union and United Nations development policies. Insects reared for the bioconversion of waste from the food sector have been increasingly explored as a source of compounds with high aggregated value. The biomass of Black Soldier Fly larvae (BSFL) contains a significant lipidic fraction, from where an oil rich in lauric (C12:0), palmitic (C16:0), linoleic (C18:2), and oleic (C18:1n-9) acids can be sourced. This fatty acid blend shows great potential in skin formulations, offering a possible alternative to plant-based materials like palm or coconut oils, which are obtained at a considerable environmental cost. Our work explores the applicability of BSFL oil extracted by hot press as the main component of emulsions.
Different oil in water (O/W) creams were prepared in this study. BSFL oil was the sole component of the oil phase, whereas different combinations were attempted in the water phase: a) Aristoflex® AVC and 2 surfactants; b) Aristoflex® AVC; c) 2 surfactants. The performance of these formulations was compared with that of an Aristoflex® AVC gel and an aqueous mixture of the 2 surfactants. All formulations were characterized in terms of pH, viscosity and organoleptic properties, and stability was tested for 60 days (25 ± 2 ° C and 60 ± 5% R.H.). Accelerated stability studies were conducted (centrifugation and thermal stress). Both the Repeated Open Application Test (ROAT) and Patch Test methodologies were employed in the in vivo compatibility studies conducted in human participants. The latter was assessed by visual scoring, whereas measurements of SC hydration, TEWL and erythema were performed during the ROAT.

Results showed that the physicochemical properties of the different formulations were suitable for skin application. Stability was achieved, both under room temperature and accelerated conditions, even in the cream without surfactants. The biocompatibility of all formulations was displayed by the two different in vivo assays.
In conclusion, our findings suggest that BSFL oil can serve as an alternative ingredient suitable for skin applications. In vivo efficacy assays are ongoing to ascertain the moisturizing and barrier restoring properties of this novel ingredient.

P54. Exploring the safety and efficacy of an upcycled Humulus lupulus extract for cosmetic applications in Atopic Dermatitis

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Atopic Dermatitis (AD), also known as atopic eczema, is a chronic and relapsing inflammatory skin disease, characterized by pruritus, xerosis, and eczematous lesions. Humulus lupulus is rich in several bioactive compounds, the described main ones being alpha and beta acids and polyphenols. The anti-inflammatory, antioxidant, and antimicrobial capacities are the most described effects of these compounds. This work aims to evaluate the safety and efficacy of an upcycled hop extract, derived from brewing industry waste. The extract was obtained from beer production trubs using solid-liquid extraction with 96% ethanol and characterized by HPLC. After extraction, the ethanol was completely evaporated, and the resulting extract was dissolved in dimethyl sulfoxide (DMSO) (Extract A) and subsequently in propylene glycol (Extract B). The microbiological quality of the extracts was assessed according to the Eur. Phar. 2.6.12 monograph. Safety was assessed by evaluating cytotoxicity through the MTT assay in human keratinocytes (HaCaT cell line) and macrophages (RAW 264.7 cells) for 24h contact time. The antioxidant capacity was assessed through the DPPH radical scavenging assay. Extract A exhibited higher cytotoxicity, being biocompatible only at 0.03% v/v in both HaCaT and RAW cells. In contrast, Extract B showed higher viability in both cell lines, being compatible at 2% v/v for HaCaT cells and 0.13% v/v for RAW 264.7 cells, suggesting that Extract B is less cytotoxic than Extract A. The antioxidant capacity of both extracts was assessed using the DPPH assay. Extract A (IC50 4.9 mg/mL) and Extract B (IC50 34.7 mg/mL) displayed a low antioxidant activity, with an Antioxidant Activity Index (AAI) of less than 0.04, indicating that neither extract possesses significant antioxidant properties. In conclusion, the results show that hop extracts, particularly Extract B, exhibit lower cytotoxicity than Extract A. Given the promising lower toxicity of Extract B, ongoing studies are investigating its potential to promote wound healing, common in Atopic Dermatitis, using a cell migration assay in HaCaT cells.
Additionally, its anti-inflammatory effects are further being explored by evaluating Nitric Oxide production in LPS-stimulated RAW 264.7 cells.

P55. Effective topical treatment of skin inflammatory diseases assisted by photoacoustic waves

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Psoriasis and atopic dermatitis are immune-mediated skin disorders, with moderate-to-severe cases often resistant to conventional topical treatments. Current therapies rely on systemic immunosuppressants such as methotrexate, which are associated with significant adverse effects. To address this limitation, we propose a novel approach using topical administration of this drug, aiming to minimize systemic toxicity and off-target metabolization.[1] Drug penetration is enhanced using photoacoustic (PA) waves, which transiently disrupt the stratum corneum, increasing skin permeability. The effectiveness of this technology has been demonstrated in previous studies. 2,3 A 0.2% (w/v) methotrexate hydrogel with suitable properties for topical application was successfully developed, achieving a drug release rate of 98.5 ± 8.5% after 24 hours. In vitro studies using porcine skin compared passive methotrexate delivery with photoacoustic-enhanced delivery. An 8-hour permeation study revealed that methotrexate absorption increased within the first hour when PA waves are applied for 5 minutes. This effect persisted throughout the study, with both conditions ultimately showing a comparable permeation profile. While long-term studies showed no significant differences in retained drug amounts in skin samples, a 1-hour deposition study indicated a progressive increase in drug delivery into the skin with longer exposure times to PA waves. Although the compound permeated through 760 µm-thick skin, suggesting potential systemic absorption, the quantities delivered into the Franz cell compartment (0.52 µg with 10-minute PA waves) were substantially lower than those administered orally (up to 30 mg/week). This suggests a reduced risk of systemic adverse effects. In vivo studies are planned to evaluate treatment efficacy and optimise the application regimen in animal models of the diseases.

Acknowledgments
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P56. Perilla Leaf-Derived Extracellular Vesicle-Like Particles: A Green and Scalable Natural Ingredient for Topical Anti-inflammatory Therapy and Cosmetic Applications

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Plant-derived nanovesicles are emerging as next-generation ingredients in topical drug delivery and skincare. In this study, we report extracellular vesicle-like particles derived from Perilla frutescens leaves (PLEVPs) as a novel green and biocompatible nanoparticle system with strong potential for treating inflammatory skin diseases and for use in functional skincare formulations. Unlike crude plant extracts, PLEVPs exhibit consistent size, structure, and bioactivity, supporting their qualification as a standardized new raw material with promising regulatory accessibility in both therapeutic and cosmetic contexts. To overcome common issues with nanoparticle instability and low skin penetration, we developed a Carbopol-based hydrogel incorporating PLEVPs. This formulation exhibited favourable rheological properties, excellent skin adhesiveness, and long-term stability over 60 days under cold storage. In vitro and in vivo release studies confirmed sustained and controlled release, while fluorescence imaging demonstrated deep dermal penetration and prolonged retention on both healthy and inflamed skin. Notably, batch consistency of PLEVPs in terms of metabolite, protein, and lipid profiles further supports their scalability for industry use. In biological assays, PLEVPs hydrogel showed robust antioxidant and anti-inflammatory activity. In IL-6-stimulated keratinocyte models, PLEVPs significantly reduced intracellular ROS levels and pro-inflammatory cytokine secretion. In a murine imiquimod-induced psoriasis-like model, topical application of the PLEVPs hydrogel alleviated erythema, reduced epidermal thickening, and improved histological scores, with no observed irritation or systemic toxicity. These therapeutic effects are not only indicative of anti-inflammatory potential but also suggest utility in restoring skin barrier function and modulating local immune responses. In conclusion, this work introduces a sustainable, well-characterized plant-derived particle system that integrates formulation science with biological efficacy. PLEVPs offer strong potential as a new class of natural topical ingredients for both dermatological treatment and green cosmeceutical development.

P57. Combining two biophysical techniques to substantiate the anti-aging claims of skin care products: AFM and SAXS coupling

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Whether for in vivo or in vitro testing, evaluating the effectiveness of the anti-aging products on the skin is a challenge. Histological observation of dermis explants is the most common in vitro technique to visualize skin morphology at macro- and micro-scale. However, it is interesting to note that aging processes, environnemental stress or pathologies can lead to a decrease in the inter- and intra-fibrillar organizations of collagen. Thus, to complete the histology and observe the possible effects at the nanoscale, Novitom has co-developed with Lipotec /Lubrizol a new ex vivo biophysical approach based on the analysis of the topography of collagen packing of fibers by Atomic Force Microscopy (AFM) coupled with the analysis of the structural intrafibrillar quality of collagen by Small-Angle X-ray Scattering (SAXS). The complementary of the two techniques allows us to assess the quality of collagen organization both at intra- and inter-fibrillar levels. On one hand, the AFM images show the cohesion between the neighbouring microfibrils, i.e. an inter-fibrillar characteristic supposed to be linked to the firmness of the tissue. On the other hand, the intensity of the X-ray diffraction peaks on SAXS patterns informs us about the quality of the 65 nm intrafibrillar longitudinal repeat along the collagen microfibrils.

The experimental protocol to evaluate anti-aging effect of a product on collagen structure starts with the treatment of explants in survival conditions during about 8 days in usual ex vivo conditions (culture medium, temperature, CO2). The treatments include explants „young" and „old" explants. The „young" explants correspond to young donors, the „old" explants being either directly linked to the age of the donor or obtained by a biochemical treatment applied to the explants of the same young donor, like phosphorylation, glycation or carbamylation. Cuts (about 20 µm thick) are then microtomed and deposited on flat supports for observations. It is worth to emphasize that none of the two techniques require specific staining.

This original approach based on two biophysical techniques provides objective structural information on collagen organizations in the dermis. It offers complementary information to histological observation, biometric measurement or OMICs study and could be linked to the mechanical properties. The sensitivity of the two techniques is good enough to allow the detection of early structural changes.

P58. Unveiling the impact of topical formulations on the organization of stratum corneum lipid barrier using X-ray micro-diffraction

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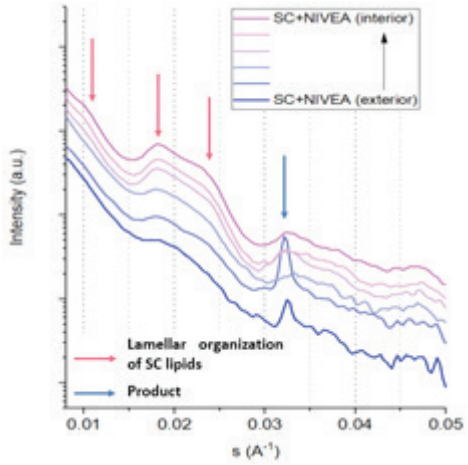
The molecular organization of the lipids of the stratum corneum (SC) plays a key role in its barrier function. Several tools are usually used to probe the organization, or rather the state, of intercorneocyte lipids, such as TEM microscopy, Raman spectroscopy or DSC calorimetric analysis, but none provide direct structural information on lipid stacks at the molecular level. X-ray diffraction is the only technique that gives direct access to molecular organizations, whether it is the lipid lamellar stacking (layer thickness, orientation) or the lateral organization of molecules within the lamellae (amorphous vs. crystalline, types and sizes of crystallized networks). This technique also provides information on the molecular organizations of product in bulk or films after application on the surface of the skin. Thanks to the exceptional qualities of X-rays provided by synchrotrons, we have succeeded in developing measurement protocols to collect data at micrometric spatial resolution (µ-XRD), and thus to obtain all structural descriptors as a function of depth in the SC.
More precisely, the information that can be extracted from a µ-XRD analysis concerns the impact of treatments on intercorneocyte SC lipid structure. This technique allows you to identify different modes of impact with treatment:

- no impact,
- penetration and merging of drug ingredients with intercorneocyte lipids,
- penetration without merging (formation of product domains inside the SC),
- changes in the crystalline amount inside the lamellae: crystallization or fluidification of the lipids
- preservation or not of the physiological lipid organization.

Data collection can be performed on isolated SC pieces after topical treatment by semi-solid or liquid formulations, or on pieces of stripped SC. For depth-based measurements, the analysis step is in the micrometer range. Measurements can be performed with a time-tracking over a few hours.



To illustrate the potential of the µ-XRD technique, observations were made on SC 1 hour after topical application of Nivea® Cream (~5 mg/cm2). The loss of signal definition from the inner to the outer surface of SC (red arrows) clearly indicates a disorganization of the lipid lamellar organization near the surface were the product was applied. In parallel, the replacement of thin arcs due to crystallized lipids inside the lamellae by a halo (data not shown) is indicative of an increase in the fluidity in the outer side. It can be concluded that this cream strongly disrupts the lipid barrier in the outer side of the SC while it has no effect in the inner side.

The impact of topical formulations on the lipid barrier organization of stratum corneum using µ-XRD has already been successfully studied for cosmetic purposes. This technique is beginning to be also used for pharmaceutical purposes, providing original and unique answers very valuable to R&D and formulation.

P59. Developing New Methods to Evaluate the Crystallinity and Solubility Behaviour of Estradiol in Pressure-Sensitive Adhesives

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Transdermal drug delivery systems (TDDS) are widely used in hormone replacement therapy. Pressure sensitive adhesives (PSAs) are a class of polymeric materials used widely in TDDS that have the ability to bond with surfaces on the application of light pressure without the need for heat or solvents[1]. The solubility and crystallisation properties of the active pharmaceutical ingredient (API) in the adhesive are critical quality attributes of drug-in-adhesive (DIA) TDDS[2].
The objective of this work was to explore a novel, high-throughput method as an alternative to microscopic slides for investigating the saturated solubility of estradiol in various PSAs. Traditional microscopy, the most prevalent method of determining API solubility in PSAs, involves applying wet blends of adhesive onto slides to visually inspect for crystal formation. However, this method has several limitations, as patch depth and drying time can affect crystal formation within the PSA[3], leading to unreliable results. Furthermore, each slide holds only one drug load, requiring numerous slides for different API/PSA combinations, making early formulation development labor-intensive and challenging to categorize and store.
Using estradiol as a model drug, "mini-patches" which systematically explored different drug loadings were produced using two PSAs, one silicone-based and one polyacrylate-based. Mini-patches were produced in chemically-compatible cyclic olefin copolymer 96-well plates at a fixed patch depth. They were then microscopically examined at various timepoints using a polarised lens to detect crystallisation over an eight-week period. Additionally, replicate patches of each drug concentration were analysed by Differential Scanning Calorimetry (DSC) to detect crystallisation as a method independent of subjective visual inspection.
Microscopic analysis revealed crystal formation in silicone patches at estradiol loadings of 1% and higher across all time points. In polyacrylate patches, crystallization appeared at 5% and higher at day 0, with 1% showing crystallization by week four, increasing with higher loadings. Using DSC, crystallisation was detected by a peak at 178 - 180°C, the melting point of estradiol[4]. This peak was observed at concentrations above 3% w/w with the silicone adhesive and was absent from polyacrylate PSA samples of all drug loadings submitted.

This study presents an alternative streamlined method for assessing estradiol solubility in PSAs, providing a standardised approach to preformulation of DIA systems.

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P60. In vivo Raman imaging of the skin

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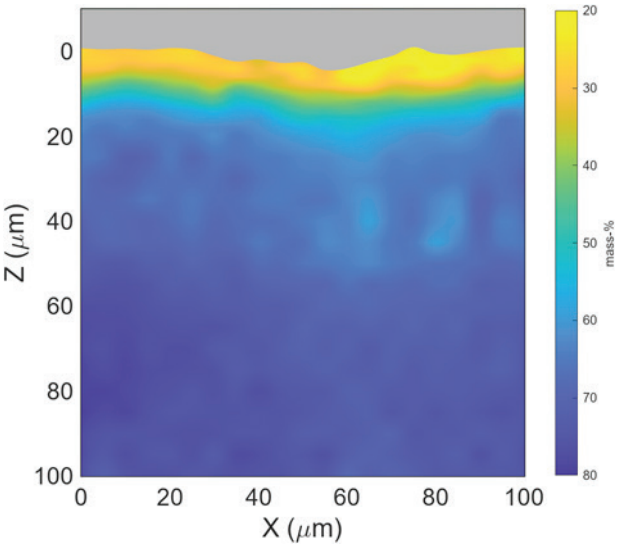
Confocal Raman spectroscopy enables in vivo measurement of concentrations of skin constituents and topical formulations with a high spatial resolution. The gen2-SCA (RiverD International, Rotterdam, The Netherlands) is a dedicated instrument for such measurements. In the past ten years the gen2-SCA has been used in numerous studies to measure concentration as a function of depth in the skin. More recently, an analysis method was added to the SkinTools data analysis suite, which enables full quantification of concentration profiles as a function of depth, in mg/g protein and in mg/cm3, as well as the determination of the total amount per cm2 skin area.
Here we present a new feature of in vivo Raman imaging of the skin, providing quantitative 2D cross-sectional images of the distribution of skin constituents and of topical products in the skin. To enable in vivo Raman imaging, the instrument must be able to record many spectra in a short time. This requires a highly sensitive Raman instrument that is fully optimized for in vivo skin measurements, such as the gen2-SCA.



Rapid Raman profiles were measured in an XZ-grid, from the skin surface to a depth of 100 μm into the skin on the volar forearm. The lateral spacing was set at 5 μm and the depth spacing at 2 to 5 μm. This resulted in the automated recording of 672 Raman spectra in a total of 9 minutes. From each spectrum the water mass percentage was quantified and an interpolated heatmap was created.

Fig. 1. In vivo Raman image of the water distribution in the skin (mass-%).

Measurement of Raman depth profiles on a grid, and presenting the concentration as 2D cross-sectional images, uniquely expands the view and possibilities of in vivo confocal Raman spectroscopy to asses the skin barrier and permeation of topical products.

P61. Catechol-Based Nanocarriers for Targeted Delivery of Tofacitinib in Alopecia Areata: Enhancing Stability and Encapsulation for Skin Applications.

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Catechols and their derivatives possess unique properties such as chelation, redox activity, and strong interactions with materials,[1] making them highly versatile for biomedical applications. Their presence in biological molecules like melanins highlights their potential in dermatology. Additionally, catechols effectively stabilize metal ions, enabling the development of Nanoscale Coordination Polymer Particles (NCPs) for targeted drug delivery. These NCPs offer high encapsulation efficiency, sustained release, and excellent stability, making them promising carriers for non-invasive treatments of skin disorders.[2]
Alopecia Areata (AA), an autoimmune disease causing hair loss, has been linked to immune dysregulation. JAK inhibitors, such as Tofacitinib, have shown promise for hair regrowth, but systemic side effects necessitate targeted delivery. In this study, we investigate the use of NCPs as vehicles for Tofacitinib to enhance its therapeutic efficacy while minimizing adverse effects. We synthesized catechol-saccharide ligands at a gram scale and explored different saccharides, such as lactose, to assess their impact on NCP stability and drug encapsulation.[3]
Tofacitinib, in its free base form, has poor water solubility, but its coordination with NCP metal cores and interactions with nitrogen donor atoms in its pyrrolopyrimidine ring significantly improved encapsulation efficiency (40–55%). Catechol-saccharide ligands facilitated drug incorporation during self-assembly, enhancing both stability and drug loading. The metal-organic nature of NCPs enabled precise control over ligand and metal ion selection.
Our formulations exhibited excellent stability in DMSO-water (5%) and DMSO-Hepes buffer for over a month, even after freezing at -20°C. Furthermore, we synthesized NCPs using both iron and zinc, with zinc being particularly relevant due to its association with autoimmune diseases and potential therapeutic role in AA.[4] The combination of high Tofacitinib encapsulation and zinc-based NCPs may lead to synergistic effects, improving treatment outcomes. Future studies will explore drug release under physiological conditions, such as pH changes and reductive environments, to optimize NCP-based delivery for autoimmune-related hair loss treatments.

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P62. Development of an antimycotic hydrogel using Quality by Design for the treatment of fungal infections

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Background: Over the past decades, stable topic formulation development has been a key focus in pharmaceutical research. Hydrogels, three-dimensional polymeric networks, offer various properties such as hydrophilicity, biocompatibility, and strong potential for different applications. These properties make them suitable for dispersing water-insoluble substances. The active pharmaceutical ingredient (API) chosen for this study, Miconazole, is a broad-spectrum antifungal agent commonly used to treat superficial mycotic infections. Objective: This study aims to develop an optimal gel formulation containing Miconazole (Mic), a poorly water-soluble active ingredient, for treating infections caused by Candida albicans and Candida parapsilosis using a D-optimal design approach. Materials and methods: Two gel series were prepared: GB1-GB7 (without the active ingredient) and GMic1-GMic7 (with Miconazole). These formulations were evaluated based on consistency, spreadability, drug content, antifungal activity, rheological behavior, and tangential stress. A D-optimal design model was applied, considering the following independent variables: Carbopol® 940 (CBP) concentration, sodium hydroxide concentration, and the presence or absence of Miconazole. The Mic-containing gels were further assessed for microbiological efficacy. Results: Among the formulations, GMic5 (0.9% CBP, 0.35% NaOH) exhibited the highest consistency, while GB2 (1% CBP, 0.3% NaOH) had the lowest. The gels exhibited pseudoplastic flow behavior, with variations based on composition. In terms of spreadability, the results ranged between 1000 mm² and 3525 mm2. The presence of Mic generated lower results for spreadability and consistency studies, while increased viscosity was observed. Moreover, higher CBP concentrations led to increased tangential stress and viscosity. Drug content across all formulations met the European Pharmacopoeia (Ph.Eur.10) acceptance limit of ±15%. Additionally, all Mic-containing formulations (GMic1-GMic7) demonstrated antifungal efficacy against Candida albicans and Candida parapsilosis. Conclusions: Critical factors affecting gel formulation were identified, with Miconazole playing a pivotal role in hydrogel creation. The formulations tested showed overall satisfactory results. Utilizing MODDE® 13.1 software, an optimized version containing 0.84% Carbopol® 940, 0.32% sodium hydroxide, and Miconazole was developed and assessed.

P63. Imiquimod nanosystems for advanced dermal delivery

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Imiquimod (IMQ) is commonly used in the treatment of actinic keratosis and precancerous skin conditions but has low bioavailability because of its poor solubility in most pharmaceutical excipients. Our study aims to enhance the bioavailability and therapeutic efficiency of IMQ with nanoparticulate formulations that exhibit skin adhesion, drug targeting to skin tissue and reduced systemic effects.
Nanosystems (liposomes, lipid nanocapsules, nanoemulsions, and nanocrystals) were prepared by standard methods such as thin lipid film hydration, high pressure and shear homogenization, or wet milling. All systems were further characterized regarding the size, morphology, encapsulation efficacy and stability. The final concentration of IMQ ranged from 0.3% in liposomes to 2% in nanoemulsion and nanocrystals. The formulations were stable for at least one month.
The ability of the nanoparticles to deliver IMQ into the skin tissue was demonstrated by ex vivo studies on porcine skin. The encapsulation of IMQ into the various nanosystems yielded different levels of efficacy. The nanoemulsion was the most efficient formulation followed closely by nanocrystals. Both formulations were even significantly more effective than a marketed cream used as a control. Therefore, the effects of these two nanoformulations on the skin barrier were characterized in detail and their mechanism of action was further studied.
In conclusion, two nanosystems, nanoemulsion and nanocrystals, were evaluated as the most efficient formulations to deliver IMQ into the skin tissue. They show comparable effects on the skin barrier integrity with recovery within 10 hours as a marketed cream.

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P64. Hydrogels, oleogels, or bigels for topical application?

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Background: Gels, widely used in pharmaceutics for their simplicity in preparation and patient compliance, have evolved significantly since their discovery in the 1960s. They are versatile semisolid systems that can incorporate a variety of active ingredients. Among recent innovations, oleogels, and hydrogels have gained attention, with studies exploring their combined form, the bigel. These formulations, particularly when used for topical drug delivery, aim to overcome the limitations of oral administration, offering a solution for poorly soluble drugs or substances with a high toxicity profile. Objective: In recent years, oleogels (O) have gained increasing interest. Therefore, the study aims to compare and analyze them with the classical alternative, hydrogels (H), while also examining the behavior of bigels (B), known for combining the properties of both lipidic and hydrophilic components. As a result, all three formulations were subjected to testing. Materials and Methods: The preformulation study concluded in preparing oleogels using sunflower oil and carnauba wax as an oil binder. Xanthan gum was the polymer used to develop the hydrogel. To ensure the aseptic quality of the preparations, Cosgard was added as an antimicrobial agent. The formation of bigels involved combining the two phases with emulsifiers, such as Tween and Span 80, using an automated mixing device. The formulations underwent various tests, including texture analysis, rheology, consistency, spreadability, and microbiological evaluation, with amiodarone concentrations determined by UV-spectrophotometry. Results: H demonstrated greater penetration resistance (28.8 mm) compared to O (29.9 mm), which exhibited a more fluid consistency. When oil was incorporated into the formulation, an irregular distribution was observed in terms of gel spread whilst adding the heaviest weight (500 g). In terms of adhesivity, the lowest force needed for detachment of the upper plate was required by the oleogel (10.63×10^{-3} N/cm^2). Rheological analysis indicated that all three bases exhibited pseudoplastic thixotropic flow. Microscopic assessment identified a crystalline microstructure in O, whereas H demonstrated a porous architecture, contributing to reduced crystal aggregation in B. Moreover, microbiological evaluation verified the absence of contaminating microorganisms. Conclusions: The research and analysis conducted on the mentioned formulations revealed key properties that suggest the differences between them can offer both benefits and drawbacks. All three gels are suitable for incorporation of pharmaceutical ingredients after further optimization following the specific characteristics of the intended product and the compatibility of the active ingredients with the excipient.

P65. Evaluation of the antioxidant capacity of a gel with lavender oil and orchid extract intended for atopic dermatitis

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Background: Antioxidants have a beneficial impact on atopic dermatitis by reducing oxidative stress and inflammation, improving skin barrier function, and alleviating symptoms. Lavender oil and orchid extract are known for their individual therapeutic properties, with lavender oil recognized for its anti-inflammatory and soothing effects, and orchid extract celebrated for its antioxidant, anti-inflammatory and moisturizing benefits. Moreover, natural products have been recently approaching outstanding benefits to treat skin diseases, which serves for the active ingredient's selection, as well as for the formulation excipient. Natural gelling agents have been extensively explored for skin formulation where hyaluronic acid and alginate have been previously reported for improving the skin hydration and barrier function. In other to develop a natural formulation designed for atopic dermatitis, the aim of the work was to study the antioxidant capacity of the gel properties and how they could benefit the treatment of compromised skin conditions. Methods: The properties of the developed gels were evaluated by extensibility, swelling and degradation assays. The antioxidant efficacy of the developed gels was previously studied in vitro using DPPH assay, a free radical compound, was prepared in 80% methanol at 0.1 mM, to react with lavender oil at concentration ranging from 0.1 to 10 mg/mL, studied alone and in combination with the other actives. Results: The gelling properties are suitable for skin delivery of natural active ingredients such as plant extracts and essential oils and the DPPH assay results indicated that lavender oil presents free-radical scavenging properties, confirming the antioxidant capacity comparable to the control. Conclusions: The developed natural formulations have demonstrated good gelling properties for skin applications and exhibiting antioxidant activity, being an interesting approach to the treatment and management of atopic dermatitis skin disorders.

P66. A Closer Look at Variability in In Vitro Permeation Tests: An Analysis Based on a Caffeine Example

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In vitro permeation tests (IVPTs) are widely used to evaluate topically applied drugs and cosmetic products. These tests allow for the study of dermatokinetic properties and their results have been shown to correlate with in vivo data. However, challenges remain regarding test reproducibility, including intra- and inter-laboratory variability. This problem is particularly noticeable for substances that permeate well through the skin, such as caffeine.
The present study aimed to analyze the variability of permeation in IVPT experiments using phosphate-buffered saline (PBS) or water-based caffeine solutions applied to human skin under infinite dose conditions, defined as >10 µL/cm².
A comprehensive literature search was conducted to identify studies reporting quantitative data on caffeine permeation through human skin into the receptor solution, along with detailed descriptions of experimental conditions, including the applied dose. In total, eight studies describing nine experiments met the inclusion criteria. The cumulative amounts of caffeine in receptor solutions over time were extracted using GetData Graph Digitizer (version 2.26). In all linear plots, the coefficient of determination (R^2) exceeded 0.93, confirming the use of infinite dose conditions.
To allow cross-study comparison, the results were normalized to an applied dose of 10 mg/cm². Additionally, missing time points were estimated using linear regression to enable consistent data analysis. In one study, reliable estimation was not possible due to the availability of only two time points.
Data from all eligible studies were combined, and mean cumulative amounts at various time points were calculated, along with standard deviations and coefficients of variation (CV). At each time point, the CV exceeded 100%, indicating high variability. Furthermore, when the calculated mean value at 24 hours after dosing was compared with the individual 24-hour values from each study, only three out of eight were within a 2-fold difference from the overall mean.
Thise analysis highlight substantial variability in IVPT results for caffeine. This underlines the need for further harmonization of experimental protocols to improve reproducibility and reliability across laboratories.

P67. Assessment of the permeation of an olive oil-based formulation with baricitinib for alopecia areata

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Background: Alopecia areata is an autoimmune disorder that causes hair loss in patches across the scalp and body. Medical treatments focus on immune suppression and hair regrowth stimulation, while the use of olive oil in managing alopecia areata capitalizes on its rich composition of antioxidants. The aim of the work was to evaluate the capacity of an squalene enriched olive oil-based formulation containing baricitinib, a Janus Kinase inhibitor, in penetrating ex vivo human skin. Methods: The oil was tested for spreadability, in vitro drug release and ex vivo permeation studies. The spreadability was assessed by placing 1 mL of the oil between two plates and the increase in spreading area was plotted as a function of the increasing weights applied. Franz diffusions cells were used for the in vitro drug release study with a dialysis membrane and PBS 7.4 – 5% Transcutol as receptor fluid. The release was determined up to 52h. The ex vivo permeation test was conducted similar to in vitro release using ex vivo human skin as the biological membrane, and the amount of Baricitinib permeated and retained in the skin was determined up to 24 h. Results: The oily formulation showed a great capacity in spreading meaning an easy application. Baricitinib was released according to a zero-order kinetic model where the drug is released at a constant rate over time. Baricitinib was retained in the skin 1.7% of the applied dose, and 1.8% permeated into the receptor fluid. Conclusions: The preliminary results of the oily formulation encourage to conduct further preclinical research to evaluate the efficacy of the formulation in an alopecia areata mice model.

P68. Rethinking Skincare: Phospholipid-Based Lamellar Systems Promote Accelerated Epidermal Barrier Repair – Results of a Pilot Study

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Emulsifiers are essential components in many skincare formulations, as they facilitate the stabilization of water and oil phases. However, their impact on the epidermal barrier remains a topic of ongoing scientific discussion. Studies suggest that certain emulsifiers can disrupt the structure and function of intercellular lipids within the stratum corneum, compromising barrier integrity and resulting in increased transepidermal water loss (TEWL) and decreased skin hydration.
In this pilot study, we investigated the effects of various skincare formulations on barrier restoration following induced damage. Therefore, the forearms of healthy volunteers were treated with a sodium lauryl sulfate (SLS)-containing shower gel to provoke controlled barrier disruption. Subsequently, different topical formulations were applied to the affected areas, and their effects on barrier restoration were assessed. Evaluation methods included electron microscopy of the intercellular lipid structures in the stratum corneum and corneometry-based measurements of skin hydration.
Our results indicate product-dependent differences in barrier regeneration efficacy. Two lamellar formulations containing a structured lipid complex based on phosphatidylcholine achieved near-complete restoration of the epidermal barrier after only four applications. In contrast, a formulation containing a non-ionic emulsifier demonstrated significantly inferior reparative performance. These differences appear to be primarily driven by variations in lipid composition and the resulting lamellar organization.
These findings underscore the critical role of emulsifier selection in skincare formulations, especially in the context of damaged skin barrier function. Lipid-based lamellar formulations free from conventional emulsifiers show superior regeneration potential. Future studies with larger sample size and more comprehensive analytical approaches are needed to validate these preliminary findings and deepen our understanding of skin barrier interactions with emulsifiers.

P69. Topical liposomes loaded with Cannonau pomace extract and quercetin: a sustainable approach for Psoriasis treatment

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Psoriasis is a chronic inflammatory skin condition characterized by erythema, irritation, and epithelial damage. Current therapies often present adverse effects, prompting interest in sustainable alternatives based on natural bioactives. Grape pomace, a winemaking side-stream, is rich in antioxidant and anti-inflammatory polyphenols, yet its therapeutic use is limited by poor solubility, bioavailability, and skin penetration. Liposomes offer a strategy to overcome these barriers by enhancing stability and controlled release.

In this study, liposomes loading Cannonau pomace extract and quercetin were developed to evaluate their potential in managing skin inflammation associated with psoriasis. Vesicles were characterised for size, charge, entrapment efficiency, and rheological behaviour. Antioxidant activity was evaluated in H_2O_2-stressed HaCaT cells, while anti-inflammatory efficacy was tested in a TPA-induced mouse model of skin inflammation.

Extract incorporation increased vesicle size from ~96 nm (empty liposomes) to ~161 nm, and up to ~172 nm when combined with quercetin. All vesicles exhibited high entrapment efficiency (³82%), negative surface charge (–45 mV), and good size stability over 12 months. In vitro, CQ liposomes restored HaCaT viability to ~93% under oxidative stress, compared to ~61% in untreated cells and ~88% with extract in dispersion. In vivo, topical application of CQ liposomes significantly reduced epidermal necrosis, hyperkeratosis, and inflammatory infiltrates, outperforming both control and non-encapsulated formulations.

These findings demonstrate that liposomes loaded with Cannonau pomace extract and quercetin are effective in reducing oxidative stress and skin inflammation. The developed formulations showed high stability and appropriate rheological characteristics, supporting their potential as sustainable, bio-based alternatives for the treatment of psoriasis. Future work should focus on optimizing synergistic compositions and scaling up for clinical translation.

P70. Impact of hydrophilic natural deep eutectic solvents on the properties and sensory attributes of carboxymethylcellulose-based hydrogels for skin application

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Natural deep eutectic solvents (NaDES), derived from biorefinery components, represent an eco-friendly and sustainable alternative to traditional organic solvents in the solubilization of pharmaceutical and cosmetic active ingredients. These biocompatible solvents can be incorporated into final products, though their properties are susceptible to change due to their strong hydrogen-bonding capabilities. This study explores the effects of incorporating two hydrophilic NaDES—composed of betaine and glycerol or citric acid and glucose into a carboxymethylcellulose (CMC)-based hydrogel [1]. Differential scanning calorimetry (DSC) analysis showed that NaDES did not alter the endothermic peak of water but removed an additional endothermic peak associated with the loosening of CMC polymer chains. Rheological testing revealed shear-thinning behaviour, with the addition of 10% wt NaDES significantly increasing the gel's viscosity at rest. The inclusion of CG caused a shift from viscous-dominant to elastic-dominant behaviour, enhancing the gel structural cohesion. Texture analysis further demonstrated that NaDES-containing gels exhibited increased hardness and elasticity. Sensory evaluations also indicated notable differences in five sensory attributes, with NaDES concentration and type playing key roles. This study highlights the complex interactions between NaDES and hydrogel, providing valuable insights for the development of innovative pharmaceutical and cosmetic formulations that combine high solvent capacity with enhanced sensory qualities.

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P71. Optimization of lipid extraction from the stratum corneum (SC)

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Lipid extraction from the SC is essential for dermatological research, providing insight into the skin lipid composition as a key parameter of skin health and barrier function [1]. Traditional extraction methods often rely on chloroform, which effectively solubilizes the long-chain fatty acids (Chain length longer than 20 carbon atoms) in the SC, but is classified as a CMR substance (carcinogenic, mutagenic, reprotoxic) [2]. The aim of this study is to identify less harmful solvents using the Conductor-like Screening Model for Real Solvents (COSMO-RS). This method is used to screen for possible drop-in replacements, reducing the need for extensive experimental trials. Additionally, the study investigates the suitability of COSMO-RS for solubility predictions of long-chain fatty acids.
To predict the solubility, different molecular geometries for each unbranched, saturated free fatty acid with a chain length from 20 to 30 carbon atoms were generated using Avogadro. COSMO-RS calculations were performed on COSMO-RS with a set of 58 different solvents provided by ORCA 6.0 program suite. The simulations predicted the solubility based on the free energy of solvation for each fatty acid combined with every solvent. The best scoring solvents were tested on porcine SC samples, followed by LC-MS analysis to evaluate extraction efficiency.
The simulations predicted a set of solvents, including diethyl ether and isopropyl ether as effective solvents for the long-chain free fatty acids. Depending on the geometry, different solvent rankings were calculated. Experimental validation with SC samples confirmed in particular the two mentioned solvents as highly effective for the extraction and separation process using LC-MS. The study demonstrates that COSMO-RS can be used as a valuable tool to predict solubility, especially in the context of solvent selection for lipid extraction. The ability to perform these calculations on standard hardware is a significant advantage, making solvent screening more accessible. However, the variation in results across different molecular geometries highlights the importance of understanding physicochemical principles to properly optimize molecular structures before conducting COSMO-RS simulations.

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P72. A systematic, fast, and miniaturized approach to compound selection for topical delivery

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The developability of active pharmaceutical ingredients (APIs) depends on their chemical properties. For oral delivery, Lipinski's Rule of Five provides a useful first guideline [1]. However, this cannot be directly applied to topical delivery because the stratum corneum is a different type of barrier than the intestinal mucosa. Most topically delivered NCE were originally optimized for peroral or parenteral use and then repurposed for topical programs. In addition to permeability, also solubility and stability are important aspects of developability [2]. As the API is typically dissolved during shelf life, chemical stability is often more critical than in peroral delivery; on the other hand, there are more options for solubilization.
The developability of 30 tyrosine kinase inhibitors and five compounds was evaluated based on solubility, chemical stability and skin penetration properties using a 35 mg approach. To assess the solubilization options for the compounds, their thermodynamic solubility was investigated in five solvents, covering different options for topical formulation design to avoid false negative results. The compound requirement for this step was 15 mg. The compounds were classified into four categories (good, moderate, difficult, unfavorable). 18 of the 30 compounds had „good" or „moderate" solubility properties and were advanced to stability and skin penetration testing.
Forced degradation studies were performed in water and under acidic, basic and oxidative conditions. Since basic pH can be avoided in most formulations and oxidation can often be mitigated by antioxidants, stability in water and acidic buffer was rated highest. Skin penetration of 23 compounds (18 plus 5 references) was tested from propylene glycol and/or DIPA (if solubility allowed) from 7 mg/mL solutions. The Hamburg Model of Skin Penetration [3] was used to study penetration into the epidermis and dermis. To improve efficacy and reduce costs, a cassette dosing approach was used with five compounds per solvent, grouping compounds based on compatibility considerations. By dosing two additional compounds also alone, it was confirmed that the cassette dosing did not affect the penetration properties. Dermal concentrations found ranged from 22 ng/mg skin to 217 ng/mg skin for propylene glycol and from 7 ng/mg skin to 409 ng/mg skin for DIPA. This approach, which required a total of only 35 mg of each compound, enabled the selection of three candidates with favorable solubility, stability and skin penetration for protype development activities.

References:
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P73. Optimization of Vasoconstrictor Assay for Evaluation of Bioequivalence of 0.1% Mometasone Furoate Ointment

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The vasoconstrictor assay (VCA), also known as the skin blanching test, is a pharmacodynamic method commonly used to evaluate the topical bioavailability and bioequivalence of corticosteroid formulations. It provides a non-invasive and regulatory-recognized approach to compare the local activity of topical corticosteroids through their capacity to induce vasoconstriction in the skin microvasculature. Considering the high potency and widespread clinical use of 0.1% mometasone furoate ointments, the development of Δa reproducible and standardized VCA method is essential to ensure accurate and meaningful comparisons across generic and reference products.

In this study, an optimized vasoconstrictor assay protocol was developed for 0.1% mometasone furoate ointment using Δa single-center, intra-subject design involving healthy adult volunteers. Various experimental parameters including application time (ranging from 1 to 6 hours), occlusion status (occlusive vs. non-occlusive), and application amount (2 mg/cm2 and 10 mg/cm2) were systematically evaluated to determine the conditions that produce the most robust and discriminative skin blanching response. Skin blanching was quantified using a chromameter by monitoring changes in a* values at multiple post-application time points.

The results indicated that there was no substantial difference in blanching response between occlusive and non-occlusive application conditions. However, variability in the extent of skin blanching was observed with respect to both application duration and dose, particularly across different subjects. These findings suggest that while the mode of application (occlusive vs. non-occlusive) may not critically influence the pharmacodynamic outcome, inter-subject variability related to exposure parameters remains a limiting factor in assay consistency. Therefore, further studies involving a larger number of volunteers are warranted to enhance the robustness and generalizability of the method. The optimized protocol nonetheless demonstrates potential as a practical tool for the evaluation of topical corticosteroid bioequivalence, particularly when standardized conditions for application time and dose can be maintained across subjects.

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