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BOOK OF ABSTRACTS

INNOV DELIVERY `22
I LUSOPHONE MEETING ON INNOVATIVE DELIVERY SYSTEMS

Welcome

CBIOS is very glad to welcome you to the 1st edition of InnovDelivery. This international virtual meeting aims to explore the theme "Nature as inspiration for innovation in Health and Well-being", bringing you the insights of leading researchers from the Lusophone world - Portugal and Brazil. The four scientific sessions will look into the future developments in nanotechnology-based delivery systems, topical and transdermal delivery, delivery technologies in cosmetics and consumer products, and innovative ingredients and sustainable strategies. This event also aims to provide all participants with new skills, networking, and new collaborations.

Thank you for attending this meeting, which we hope will be an opportunity to learn and exchange ideas!

The Organizing Committee

June 2022

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This meeting was funded by national funds through FCT - Foundation for Science and Technology, I.P., under the EXPL/BTM-MAT/0112/2021, EXPL/OCE-ETA/1109/2021, UIDB/04567/2020, and UIDP/04567/2020 projects.

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General information

The meeting will be 100% virtual.

The time zone in Portugal is GMT+1.

The speakers should enter the Zoom meeting 15 minutes before their presentation and should respect the time slot for each type of communication.

Types of communication

Keynote speakers (K): 25 minutes + Q&A

Oral communications (OC): 15 minutes + Q&A

Flash communications (FC): 4 minutes + Q&A

Posters (P): AudioSlides (5 minutes)

Poster Sessions

There will be two poster sessions, at 10:40 am and 14:50 pm.

To access the posters, please click on the YouTube link available for each poster.

The Book of Abstracts of InnovDelivery'22 will be published in the Biomedical and Biopharmaceutical Research Journal, upon authorization granted by the authors.

Program	
09:00 – 09:15	Opening Session
T1: Nanotechnology-based Delivery Systems	
09:15 – 09:45	**K1:** Salette Reis LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Combinatory strategies for the development of nanocarriers to improve drug efficacy"
09:45 – 10:05	**OC1:** Adriana Cruz iBB and i4HB, Instituto Superior Técnico, Universidade de Lisboa "PURE dendrimers against cancer cells: when mitochondria are the key player"
10:05 – 10:25	**OC2:** Andreia Granja LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Folate-targeted lipid nanoparticles as promising nanocarriers for the selective delivery of mitoxantrone to breast cancer cells"
10:25 – 10:30	**FC1:** Vera M. S. Isca CBIOS, Universidade Lusófona "Nanosystem of royleanone diterpenoids from *Plectranthus* spp to improve targeted delivery into cancer cells"
10:30 – 10:35	**FC2:** Andreia Marinho LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Hyaluronic acid conjugated pH-sensitive liposomes as a promising platform delivery for prednisolone"
10:35 – 10:40	**FC3:** Tânia Moniz LAQV, REQUIMTE, Universidade do Porto "Polymeric nanoparticles for advanced delivery of 3,4-hydroxypyridone chelators and iron(III) chelates"
10:40 – 11:00	Coffee break & Poster Session

Program	
T2: Topical and Transdermal Delivery Systems	
11:00 – 11:30	**K2:** Majella E. Lane UCL School of Pharmacy, United Kingdom "Application of Confocal Raman Spectroscopy in topical formulation development"
11:30 – 11:50	**OC3:** Ana Júlio CBIOS, Universidade Lusófona "TransfersomILs: an innovative combination between transfersomes and Ionic Liquids"
11:50 – 12:10	**OC4:** Ana Isabel Barbosa LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Betamethasone-loaded hybrid hydrogels to manage atopic dermatitis"
12:10 – 12:15	**FC4:** Thaisa C. de Oliveira Federal University of Pernambuco, Brazil "Evaluation of transdermal permeation of phthalate angico gum nanoparticles containing nevirapine in microneedles"
12:15 – 12:20	**FC5:** Catarina V. Moreira Escola Superior de Saúde, Instituto Politécnico da Guarda "New approaches in the treatment and management of rosacea: a review"
12:20 – 12:25	**FC6:** João Vieira CBIOS, Universidade Lusófona "Optimization of ibuprofen-loaded transfersomes for transcutaneous delivery"
12:25 – 13:30	Lunch Break

Program	
T3: Delivery Technologies in Cosmetics and Consumer Products	
13:30 – 14:00	**K3:** Gislaine R. Leonardi UNICAMP, Brazil "Iontophoresis and liquid crystal emulsions as strategies to improve the effectiveness of formulations"
14:00 – 14:20	**OC5:** Sofia A. Costa Lima LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Exploiting smart delivery systems to slow down skin ageing"
14:20 – 14:40	**OC6:** Sara Bom iMed.ULisboa, Faculdade de Farmácia, Universidade de Lisboa "3D printing the next technology in cosmetics: personalization of skincare"
14:40 – 14:45	**FC7:** Mariane M. Vergilio UNICAMP, Brazil "Comparative effect on the skin hydration at different hyaluronic acid delivery systems"
14:45 – 14:50	**FC8:** Raquel P. Costa LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto "Quercetin-loaded lipid nanoparticles with improved antioxidant capacity potential for skin applications"
14:50 – 15:15	Coffee break & Poster session

Program	
T4: Innovative Ingredients and Sustainable Strategies	
15:15 – 15:45	**K4:** Luís C. Branco Universidade NOVA de Lisboa "Sustainable drug formulations based on ionic systems for pharmaceutical applications"
15:45 – 16:05	**OC7:** Cíntia Almeida CBIOS, Universidade Lusófona "Development of lipid nanoparticles from *Hermetia illucens* larvae extract for dexamethasone delivery for topical application"
16:05 – 16:25	**OC8:** Bojan Kopilovic CICECO, Universidade de Aveiro "Gellable aqueous biphasic systems for biopharmaceuticals encapsulation"
16:25 – 16:30	**FC9:** Luíse L. Chaves Federal University of Pernambuco, Brazil "Application of placket-burman design in the development of phthalated Angico gum nanoparticles loaded with nevirapine"
16:30 – 16:35	**FC10:** Fabiana Vieira Lima University of Espírito Santo, Brazil "Evaluation of the photoprotective potential of *Schinus terebinthifolia raddi* (rose pepper) in cosmetic formulation"
16:35 – 16:40	**FC11:** Márcia Santos Filipe CBIOS, Universidade Lusófona "Antioxidant essential oils as innovative ingredients in facial masks"
16:40 – 16:50	Awards & Closing Session

Poster Session

P1: Gabrielle Bangay
CBIOS, Universidade Lusófona

"Self-assembly nanoparticles of bioactive compounds isolated from *Plectranthus spp.*"

P2: Márcia Santos Filipe
CBIOS, Universidade Lusófona

"Medicinal Centauri Honey: a Innovative Ingredient?"

P3: Nuno Martinho
iBB and i4HB, Instituto Superior Técnico, Universidade de Lisboa

"Polyurea (PURE) dendrimers as modulators of membrane permeability to enhance cisplatin delivery"

P4: Filipa A. Soares
LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto

"Bovine Milk Exosomes: A Comparative Study of Different Isolation Methods"

P5: Yong Sze Ong
School of Pharmacy, Monash University Malaysia

"A systematic review of the emerging 5-fluorouracil nanotheranostic agents for cancer treatment"

P6: Carlota Nascimento and Mariana Santos
ECTS, Universidade Lusófona

"Development of lipid nanoparticles based on fatty acids to promote healthy skin regeneration"

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Poster Session

P7: Diana Araújo
i4HB and UCIBIO, Universidade NOVA de Lisboa
"Chitin-Glucan Complex Hydrogels: Optimization of Gel Formation and Demonstration of Drug Loading and Release Ability"

P8: Sandra Mota
UCIBIO and i4HB, Faculdade de Farmácia, Universidade do Porto
"Antioxidants from agro-industrial waste: valorisation for the cosmetic industry"

P9: Ana Júlio
CBIOS, Universidade Lusófona
"O/W emulsions containing glycinate-based ILs and phenolic compounds"

P10: António Barreira
LAQV, REQUIMTE, Universidade NOVA de Lisboa
"Ionic and Aerogel Levothyroxine formulations for drug delivery"

P11: Andreia Reis and Inês Martins
ECTS, Universidade Lusófona
"Impact of the loaded phytochemical on TransfersomILs performance"

P12: Catarina Pereira-Leite
CBIOS, Universidade Lusófona
"Advanced natural formulations to tackle skin ageing"

Keynote speakers

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K1: Salette Reis

LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto

"Combinatory strategies for the development of nanocarriers to improve drug efficacy"

Salette Reis is a full Professor at the Faculty of Pharmacy of University of Porto and the coordinator of NanoPlatforms Research Group of LAQV, REQUIMTE. SR research has been focused on biophysics and pharmaceutical chemistry, namely in the use of biomimetic membrane models to study the effect of drugs on biological membranes, establishing a relationship between this effect and their activity/mechanism of action. The development of drug delivery nanosystems to overcome the disadvantages of classical therapies is also a current research field. SR is co-author of more than 280 peer-reviewed publications in international journals and 23 book chapters. In the last 5 years, SR has been part of the research team of 6 projects (Co-PI of 3). SR successfully supervised 14 PhD students and at the moment, she is the supervisor of 3 PhD students and the co-supervisor of 3 PhDs and 5 MScs. SR is Co-Director of the International Doctoral Programme BiotechHealth (ICBAS/FFUP). SR has also organized several scientific courses: Advanced Course on Biological Barriers – In vitro biological barrier models for Health Sciences Applications; Advanced Course on Binding Assays – Protein-ligand interactions: From theory to practice and Membrane Biophysics: Impact of Lipids on Health, Disease and Therapy.

K2: Majella E. Lane

UCL School of Pharmacy, United Kingdom

"Application of Confocal Raman Spectroscopy in topical formulation development"

Majella holds a degree in pharmaceutical science and a PhD in membrane transport. Her major areas of expertise include delivery of actives to and through the skin, biophysical approaches towards the elucidation of active-skin and formulation-skin interactions, mechanisms of active absorption in skin and topical formulation design and evaluation. To date she has published more than 170 peer-reviewed papers, supervised 30 PhD students, and mentored 15 postdoctoral research associates. Majella also acts as a consultant to many multinational companies. She is the Editor-In-Chief of the International Journal of Cosmetic Science and she serves on the editorial board of a number of cosmetic and pharmaceutical science journals. In 2020 Majella was appointed to the Council of the Society of Cosmetic Scientists of the United Kingdom. Her research group collaborates worldwide and she also hosts visiting scientists from academia and industry in her laboratory.

K3: Gislaine R. Leonardi

UNICAMP, Brazil

"Iontophoresis and liquid crystal emulsions as strategies to improve the effectiveness of formulations"

Graduated in Pharmacy (1989-1993); Master's (1995 – 1997) and PhD in Pharmaceutical Sciences (1998-2000). Professor at Faculty of Pharmaceutical Sciences, UNICAMP, Brazil. Professor of the COSMETOLOGY FOR AGING WITH HEALTH AND BEAUTY course, which is offered for free by the Coursera platform, in the Portuguese language. Author of books and scientific publications in the area of development and evaluation of cosmetic and dermatological products.

K4: Luís C. Branco

Universidade NOVA de Lisboa

"Sustainable drug formulations based on ionic systems for pharmaceutical applications"

Luis C. Branco is an Assistant Professor in Nova School of Science and Technology (FCT-NOVA) and Principal Investigator at LAQV-REQUIMTE. Dr. Branco´s research interests include the development of sustainable and designer materials (e.g. ionic liquids, deep eutectic solvents and porous/polymeric ionic materials) for application in pharmaceutical chemistry, catalysis, energy and material science. He already published more than 145 scientific articles (h-index = 38; >5500 citations; https://laqv.requimte.pt/people/63-luis_alexandre_almeida_fernandes_cobra_branco, 13 book chapters and 11 patents.

Oral communications

OC1

PURE dendrimers against cancer cells: when mitochondria are the key player

Adriana Cruz[1*], José Barbosa[1], Nuno Bernardes[1], Nuno Martinho[1], Rita F. Pires[1], Sandra N. Pinto[1], Vasco D.B. Bonifácio[1,2]

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Despite the many efforts made on anticancer drug development in the last years, new strategies are still required to overcome critical issues, such as resistance and off-target effects, existing on current therapies. Cancer cell membranes, in contrast with healthy cells, are enriched in negatively charged species as result of phosphatidylserine accumulation and the presence of high levels of sialic acid on membrane glycoproteins. This high charge density is shared with bacterial membranes, raising the hypothesis that cationic agents such as antimicrobial peptides (AMPs) and synthetic mimics of antimicrobial peptides (SMAMPs) can act as potential anticancer drugs, thus sharing the same mode of action.

Herein, we demonstrate the intrinsic anticancer activity of two novel core-shell cationic dendrimers prepared from polyurea dendrimers precursors [1] Both dendrimers act through interactions with negatively charged surface groups, and our observations regarding the mechanism of action allow us to hypothesize that these dendrimers are possibly targeting the mitochondrial membrane **(Figure 1)** and consequently activating the intrinsic pathway of apoptosis. Importantly, cationic core-shell polyurea dendrimers have shown unique and rather attractive properties for potential cancer nanotherapeutics, such as lower cytotoxicity and hemocompatibility.

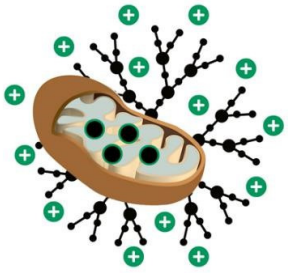

Figure 1 – Cationic core-shell dendrimer mitochondria targeting

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References [1] Restani, R.B., Morgado, P.I., Ribeiro, M.P., Correia, I.J., Aguiar-Ricardo, A. and Bonifácio, V.D.B. (2012), Biocompatible Polyurea Dendrimers with pH-Dependent Fluorescence. *Angew. Chem. Int. Ed.*, 51: 5162-5165. https://doi.org/10.1002/anie.201200362

OC2

Folate-targeted lipid nanoparticles as promising nanocarriers for the selective delivery of mitoxantrone to breast cancer cells

Andreia Granja[1], Cláudia Nunes[1], Célia T. Sousa[2,3] and Salette Reis[1]

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Breast cancer is the principal cause of cancer-related deaths in women around the world (1). Due to their non-selective tumor distribution, standard chemotherapeutic regimens often result in dose-limiting adverse side-effects and diminished treatment efficacy. Nanomedicine is a promising approach to improve the efficacy of common chemotherapeutics. Given their biocompatibility, low-cost manufacture and stability, lipid nanoparticles, such as solid lipid nanoparticles (SLN), have a great potential for drug delivery and translation into clinics (2). In this work, SLN entrapping the antineoplastic drug Mitoxantrone (Mito) were developed and functionalized with a folic acid (FA) ligand to improve tumor selectivity and minimize the systemic side-effects of the drug. SLN presented adequate physicochemical properties and excellent hemocompatibility, suggesting their suitability for intravenous administration. Additionally, they remained stable for at least 6 months. Moreover, FA-decorated SLN enhanced the anti-cancer effect of the free drug, as assessed by the IC_{50} of the nanoformulation and the induction of apoptosis in MCF-7 cells. Moreover, the functionalization resulted in a higher cancer cellular internalization, demonstrated by both confocal microscopy and flow cytometry. This cellular uptake occurred via macropinocytosis and clathrin-mediated endocytosis, suggesting the involvement of the folate receptor (FR) in this cellular uptake. Overall, these results highlight the potential of the developed SLN as promising nanocarriers for the selective delivery of Mito to breast cancer cells.

Acknowledgements: Fundação para a Ciência e Tecnologia and Ministério da Ciência, Tecnologia e Ensino Superior through the project UIDB/50006/2020 and HEALTH-UNORTE I&D&I project. AG acknowledges FCT for the PhD grant SFRH/BD/130147/2017. CN is thankful to FCT for the investigator Grant (IF/00293/2015). CTS thanks FCT for the Investigator Grant (IF/01159/2015) and to the program Atraccion de Talento (CAM), ref. 2020-T1/IND-19889 and the UE's Horizon 2020 program under the Marie Sklodowska-Curie grant no. 734801.

References

1. Sung, H., *et al*. (2021). *CA: a cancer journal for clinicians* 71(3): 209-249.
2. Granja, A., *et al.* (2021). *International Journal of Pharmaceutics 607*, 121044.

OC3

TransfersomILs: an innovative combination between Transfersomes and Ionic Liquids

Ana Júlio[1,2], João Guilherme Costa[1], Catarina Pereira-Leite[1,3,#] and Tânia Santos de Almeida[1,4,#]

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Ionic liquids (ILs) have various valuable properties, which justify their incorporation for the development of more efficient delivery systems. Additionally, nanovesicular systems, such as transfersomes, are promising to upgrade cutaneous delivery but still present some challenges ahead (1). So, our goal was to evaluate the applicability of ILs combined with transfersomes to upgrade the cutaneous delivery of rutin, a sparingly soluble drug (2).
First, it was performed a Box–Behnken factorial design to optimize the nanovesicular system to load rutin. Then, TransfersomILs containing imidazole-based ILs, cholinium-based ILs, or their combinations were produced and characterized. These innovative nanosystems were prepared considering the impacts of the ILs and their combinations on the viability of HaCaT cells and on the aqueous solubility of rutin.
The results showed that TransfersomILs present appropriate physicochemical properties for cutaneous application. Moreover, the incorporation of ILs in transfersomes improved the association efficiency, the total amount of drug released, and the storage stability of the nanosystems. Thus, ILs paved the way for the development of innovative TransfersomILs with suitable properties for cutaneous delivery.

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References

1. Caparica, R., Júlio, A., Fernandes, F., Araújo, M.E.M., Costa, J.G., Santos de Almeida, T. (2021). Upgrading the Topical Delivery of Poorly Soluble Drugs Using Ionic Liquids as a Versatile Tool. *International Journal of Molecular Sciences,* 22, 4338. DOI: 10.3390/ijms22094338.

2. Júlio, A., Costa, J.G., Pereira-Leite, C., Santos de Almeida, T. (2022). TransfersomILs: From Ionic Liquids to a New Class of Nanovesicular Systems. *Nanomaterials*, 12, 7. DOI:10.3390/nano12010007.

OC4

Betamethasone-loaded hybrid hydrogels to manage atopic dermatitis

Ana Isabel Barbosa[1, 2]; Sofia Costa Lima[1] and Salette Reis[1]

[1] LAQV, REQUIMTE, Faculty of Pharmacy, University of Porto, Portugal.

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Atopic dermatitis (AD) is a severe inflammatory skin disorder, affecting children and adults worldwide. The current treatment of severe AD focus on immunosuppression with oral corticosteroids or cyclosporine A, but associated side effects on prolonged systemic therapy compromises the treatments' effectiveness. Even though there are several treatments for AD, it is necessary to find new alternative therapies to address the numerous manifestations of the disease. Hydrogels may represent a good tool to treat AD due to their high-water content that regulates dry skin conditions, their structure versatility, ability to carry and give purpose to all kinds of drugs, capacity to be modulated and responsive to stimuli, making them excellent candidates for drug delivery vehicles in skin research. In fact, some years ago it was given importance not only to the molecule used for the treatment but also to the vehicle, and for which properties might be determinant in the success of the treatment and patient adherence to the therapy. This work aims to develop and characterize marine polymer-based hydrogels for cutaneous delivery of betamethasone to manage AD with high skin retention and low systemic spread. Two essential oils (bergamot oil and menthol) were also incorporated into the hydrogels to assess their ability to improve skin penetration. Rheological properties revealed pseudoplastic behaviour of the hydrogels, favourable characteristic for skin application. The *ex vivo* skin permeation assay showed that hydrogels promote the retention of betamethasone in skin, independently of the use of other enhancers in the hydrogel composition. Biocompatibility towards L929 fibroblasts and HaCaT keratinocytes was determined, revealing a safe usage of the hydrogels up to 100 mg mL^{-1} in the hydrogel, corresponding to 20 µg mL^{-1} in betamethasone, but was compromised by the presence of the essential oils in the higher tested concentrations. Given their high-water content might be a good strategy to overcome the characteristic dryness in AD skin. The designed hydrogels are biocompatible and promote the retention of betamethasone in the skin with low permeation, suggesting their potential as platforms to treat skin inflammatory conditions.

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OC5

Exploiting smart delivery systems to slow down skin ageing

Renata Basto, Tânia Moniz, Cláudia Nunes, Sofia A Costa Lima* and Salette Reis

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Skin ageing is induced by both intrinsic and extrinsic factors, namely solar ultraviolet (UV) radiation. The current increased levels of UV radiation provoke early skin ageing, which in turn impairs the protective ability of the skin and leads to various diseases, including skin cancer. Biological mechanisms of skin ageing involve the action of reactive oxygen species, genetic mutations, as well as hormonal changes.
Resveratrol belongs to the large group of biologically active polyphenolic compounds while niacinamide is an amide form of vitamin B3, both exhibit remarkable anti-ageing properties. Yet, their physicochemical properties difficult for an effective skin delivery per se. Here two different smart delivery systems were designed and evaluated to improve resveratrol and niacinamide skin delivery. For resveratrol, topical delivery polymeric microneedles (MNs) made from alginate per ser or mixed with k-carrageenan (k-CRG) were developed. Resveratrol-loaded MNs were obtained using the micromoulding technique and structurally characterized revealing adequate shape and mechanical strength to pierce the skin. Skin permeation studies showed that both MNs types have a similar compound release profile, allowing the retention of drug in the skin as desired for a topical application. In sum, the most suitable formulation for resveratrol topical application is the alginate-based MN, since this device allowed the most adequate permeation profile for RSV concomitantly exhibiting the highest strength to pierce the skin. For niacinamide skin delivery a hybrid nanogel was designed using k-CRG and poly-vinylpyrrolidone polymers combined with jojoba oil, as a permeation enhancer. Three different types of transethosomes were prepared by the thin-film hydration method, distinct by the presence of either an edge activator or a permeation enhancer, to allow a drug-controlled delivery. The hybrid hydrogels exhibited robust, porous, and highly aligned macrostructures, and when present, jojoba oil has changed their morphology. Skin permeation studies with transethosomes-loaded hydrogels showed that nanogels per se exhibit a more controlled and enhanced permeation, in particular, when jojoba oil was present in the transethosomes. These promising nanogels protected the Human keratinocytes from UV radiation thus, can be added to sunscreens or after-sun lotions to improve skin protection.

Acknowledgments: This work received financial support from PT national funds (FCT/MCTES) through grant UID/QUI/50006/2020. TM, CN, and SCL thank grants (POCI-01-0145-FEDER-030834, IF/00293/2015, CEECIND/01620/2017, respectively) financed by European and National funds.

OC6

3D printing the next technology in cosmetics: personalization of skincare

Sara Bom[1], Marta Ferreira[2], Catarina Santos[1,2,3], Ricardo Cláudio[1,2], Pedro C. Pinto[1,4], Helena M. Ribeiro[1] and Joana Marto[1]

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Introduction: The opportunity to produce cosmetic products by semi-solid extrusion 3D printing has been explored as a way of offering solutions to personalize skincare products, which represents a market trend (1). Therefore, the main goal of this work was to develop an innovative and versatile gelatin-based 3D printed patch with controlled network topology for multipurpose cosmetic applications, like anti-aging, that can be easily personalized by changing different print parameters.

Materials and Methods: 3-layered gelatin-based patches with several infill patterns were printed in an extrusion-based 3D bioprinter (Allevi2, USA), varying the line distance and the angles. Measurements of pore width were performed in the ImageJ® software and Visioscan® was used to record the topography. After, Visia-CR™ was employed as a 2D skin scanner for designing a personalized eye patch with controlled network topology.

Results and Discussion: Gelatin-based patches with different degrees of porosity were successfully printed, showing great applicability in terms of modulating the release of bioactive substances. As a proof-of-concept, the anti-aging fluorescent purified tomato extract, IBR-TCLC® in Jojoba Oil 0705, was incorporated into the personalized eye patch. Topographic analysis suggested that the printing accuracy and pore shape fidelity were not largely affected by its incorporation, which reinforces the versatility of the technology employed. Additional data also showed that it is possible to visualize and record the fluorescence of the bioactive incorporated on the Visia-CR™.

Conclusion: The 3D printing approach employed opens a new prospective to produce personalized skincare products for different cosmetic applications. Moreover, the possibility to evaluate *in vivo* the porosity effect on the bioactive release is being tested.

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References

1. Bom, S., Martins, A. M., Ribeiro, H. M., & Marto, J. (2021). Diving into 3D (bio)printing: A revolutionary tool to customize the production of drug and cell-based systems for skin delivery. International Journal of Pharmaceutics, 605, 1–20. Doi: 10.1016/j.ijpharm.2021.120794

OC7

Development of lipid nanoparticles from *Hermetia illucens* larvae extract for dexamethasone delivery for topical application

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Nanotechnology has provided promising and advanced tools for the delivery of drugs and actives for topical application. Fatty acids (FA) are critical in skin barrier function and the development of lipid nanoparticles made up of FA compatible with those present in the epidermis may be a good strategy for the treatment of diseases related to skin barrier impairment (1). The lipid extract from *Hermetia illucens* larvae, a blend of FA that is composed mainly by saturated FA (2), can be a potential ingredient to prepare nanodelivery systems based on innovative natural raw materials. The present work aimed to optimize the composition of lipid nanoparticles and the critical steps of their production methods using the lipid extracts obtained from *H. illucens* larvae biomass for the delivery of dexamethasone for topical application.

Solid lipid nanocarriers (SLN) were prepared with different amounts of lipid extract, surfactant and considering the maximum solubility of dexamethasone in the lipid extract. After the addition of the aqueous phase after melting the lipid phase, the nanoparticles were homogenized by ultrasonication. The characterization of the nanoformulations was performed after cooling at room temperature, in terms of particle size, polydispersity index (PDI), and zeta potential. The encapsulation efficacy and loading capacity of the nanoparticles were also evaluated.

The unloaded lipid extract of the larvae provided nanoparticles with sizes under 155 nm, a PDI<0.25 and promising zeta potential values < -40 mV. The lipid nanoparticles loaded with dexamethasone provided nanoparticles with similar characteristics and also presented satisfactory results in terms of the encapsulation efficacy (ca. 84%). Our results suggest that the SLN made of crude lipid extract from *H. illucens* larvae can be a promising strategy for nanoparticles development for drugs encapsulation, which can be combined with an emollient effect due to its lipidic content and, thus, promoting skin barrier recovery. After these initial studies, a quality-by-design (QbD) approach - BoxBehnken factorial design - will be employed and the optimized nanoformulation to load dexamethasone will be fully characterized.

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References

1. Almeida, C.; Filipe, P.; Rosado, C.; Pereira-Leite, C. (2022). Nanodelivery Strategies for Skin Diseases with Barrier Impairment: Focusing on Ceramides and Glucocorticoids. *Nanomaterials*, 12, 275. doi: 10.3390/ nano12020275

2. Spranghers, T.; et al. (2017). Nutritional composition of black soldier fly (*Hermetia illucens*) prepupae reared on different organic waste substrates. *J. Sci. Food Agric.* 97, 2594–2600. doi: 10.1002/jsfa.8081.

OC8

Gellable aqueous biphasic systems for biopharmaceuticals encapsulation

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Biopharmaceuticals developed with recombinant or hybridoma technology have the potential to treat a wide range of diseases, although they are not without limitations. Because they are proteins, many biopharmaceuticals lose their stability quickly in commercial formulations. With the rapid growth of protein-based pharmaceutical products over the last decade, one of the most difficult tasks in product development has been ensuring protein structural stability during purification, processing, and storage. Furthermore, protein instability is a significant obstacle to the more desirable oral administration of protein therapeutics. If proteins are to be used as therapeutics, they must be effectively stabilized and preserved at a high quality for an extended period of time. If they are not stabilized, their therapeutic efficacy falls, which demands the development of appropriate formulations and delivery methods.
This work offers a new approach using an already existing platform in order to avoid biopharmaceutical denaturation. A unique encapsulation approach was developed using aqueous biphasic systems (ABS) containing phase-forming components with gelling capabilities. For microdroplet manufacturing, an emulsification method based on gelatin was investigated. Biopharmaceutical encapsulation, release profile in simulated gastric fluids, and stability have been determined.

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Flash communications

FC1

Nanosystem of royleanone diterpenoids from *Plectranthus* spp to improve targeted delivery into cancer cells

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Nature is the most important source of novel pharmacologically active compounds for cancer treatment. *Plectranthus* genus (Lamiaceae) has been widely used in traditional medicine and seems to be promising for the research of new drug leads. In fact, *Plectranthus* spp. are rich in cytotoxic diterpenoids, such as the 6,7-dehydroroyleanone (DeRoy) and the 7α-acetoxy-6β-hydroxyroyleanone (Roy). (1) Royleanone diterpenoids are commonly very low water-soluble compounds and nanotechnology can be employed to improve drug solubility and targeted delivery: moreover, nanoformulations are often able to decrease the most frequent side effects associated to chemotherapy. (2) Hybrid nanoparticles of DeRoy have shown an increased efficacy of the natural royleanone on NCI-H460 and NCI-H460/R cell lines. (3) Additionally, self-assembling nanoparticles combined with Roy reduced the cytotoxicity against normal cells (Vero-E6) compared to parent compound (Roy) and displayed a low release of Roy at physiological pH. (2) These results suggest that nano-assemblies of royleanones may act as a promising anticancer strategy.

In this report, we describe the extraction and isolation of Roy from P. *grandidentatus*. Also, Roy was derivatized with the goal of improving its antitumoral proprieties. Several derivatives were prepared with overall good yields and are currently under *in vitro* antitumoral evaluation. So far, two benzoylated derivatives revealed promising cytotoxic properties to be further exploited in nanoformulations. Overall, we expect that derivatives in nanosystems can improve the drug delivery and lead to an enhanced anticancer activity.

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References

1. Matias, D., Nicolai, M., Saraiva, L., Pinheiro, R., Faustino, C., Diaz Lanza, A., . . . Rijo, P. (2019). Cytotoxic Activity of Royleanone Diterpenes from Plectranthus madagascariensis Benth. *ACS Omega*, 4(5), 8094-8103. doi:10.1021/acsomega.9b00512

2. Ntungwe, E., Domínguez-Martín, E. M., Bangay, G., Garcia, C., Guerreiro, I., Colombo, E., . . . Rijo, P. (2021). Self-Assembly Nanoparticles of Natural Bioactive Abietane Diterpenes. *Int J Mol Sci*, 22(19). doi:10.3390/ijms221910210

3. Garcia, C., Silva, C. O., Monteiro, C. M., Nicolai, M., Viana, A., Andrade, J. M., . . . Rijo, P. (2018). Anticancer properties of the abietane diterpene 6,7-dehydroroyleanone obtained by optimized extraction. *Future Med Chem*, 10(10), 1177-1189. doi:10.4155/fmc-2017-0239

FC2

Hyaluronic acid conjugated pH-sensitive liposomes as a promising platform delivery for prednisolone

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Inflammation is a biological defense process of the body, which when not properly regulated can lead to chronic inflammatory disorders, such as rheumatoid arthritis or osteoarthritis. Fortunately, there is already a wide range of drugs that aim to control these pathologies and, consequently, inflammation. Within this range of drugs, prednisolone is considered by the World Health Organization (WHO) as an essential anti-inflammatory. (1) However, its long-term use is limited due to the adverse effects associated with it. In the struggle to overcome these limitations, drug delivery systems emerge, where liposomes play a prominent role due to the advantages they present. Thus, in this study, pH-sensitive liposomes were developed for targeted administration of prednisolone. (2) As a way to target the liposomes to the CD44 receptor, overexpressed by activated macrophages (3), functionalization with hyaluronic acid was considered.

Liposomes, produced by the thin-film hydration method, were characterized in terms of hydrodynamic diameter, polydispersity index, zeta potential, and encapsulated efficiency. Its biocompatibility was evaluated by in vitro cytotoxicity studies (L929, RAW 264.7, and THP-1 cell lines) and by hemolysis studies. The ability of liposomes to regulate the release of inflammatory mediators was also verified.

Overall, the liposomes revealed to be a promising nanotherapy to enhance the therapeutic efficacy and efficiency of prednisolone on chronic inflammation long-term treatment.

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References

1. WHO. *22nd World Health Organization Model List of Essential Medicines*. 2021 [retrieved 2022 May 12]; https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02

2. Gouveia, V., Lopes-de-Araújo, J., Lima, S.A.C., Nunes, C., Reis, S. (2018). Hyaluronic acidconjugated pH-sensitive liposomes for targeted delivery of prednisolone on rheumatoid arthritis therapy. *Nanomedicine*. 13:1037. doi:10.227/nnm-2017-0377

3. Marinho, A., Reis, S., Nunes, C. (2021). Hyaluronic Acid: A Key Ingredient in the Therapy of Inflammation. *Biomolecules*. 11:1518. doi:10.3390/biom11101518

FC3

Polymeric nanoparticles for advanced delivery of 3,4-hydroxypyridone chelators and iron(III) chelates

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Ligands from 3-hydroxy-4-pyridinones (3,4HPO) family and their chelates offer many advantages such as synthetic versatility, low toxicity, and efficiency in a variety of fields of applications (1). Particularly, 3,4HPO and their iron(III) chelates (Fe-3,4HPO) have been described in the last years as promising scaffolds for the development of new antibacterials (1) and plants' fertilizers (2), respectively.

Our investigations pointed out the relevance of rhodamine functionalization of these ligands to reach the biological target and fight *Mycobacterium avium* infection (1).

Additionally, last results revealed that Fe-4,3HPO are suitable to be used as new agents to correct Iron Deficiency Chlorosis in soyabean plants (2).

However, further studies are required to improve the efficacy of both chelates and Fechelates and reduce the eventual toxicity of the previously found promising structures. Aiming this, nanotechnology concepts have been applied to the development smart delivery systems to encapsulate the active agents, thus improving their bioavailability. Herein we will present our last findings regarding the design and characterization of novel polymeric nanoparticles considered to successfully encapsulate and delivery the lead molecules.

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References

1. Rangel, M., Moniz, T., Silva, A.M.N. and Leite, A. (2018). Tuning the anti(myco)bacterial Activity of 3-Hydroxy-4-pyridinone Chelators through fluorophores, *Pharmaceuticals*, 11, 110133. Doi: 10.3390/ph11040110

2. Santos, C. S., Rodrigues, E., Ferreira, S., Moniz, T., Leite, A., Carvalho, S. M. P., Vasconcelos, M. W. and Rangel, M. (2021). Foliar application of 3-hydroxy-4-pyridinone Fe-chelate [Fe(mpp)$_3$] induces responses at the root level amending iron deficiency chlorosis in soybean, *Physiologia Plantarum*, 1-11. Doi: 10.1111/ppl.13367

FC4

Evaluation of transdermal permeation of phthalate angico gum nanoparticles containing nevirapine in microneedles

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Transdermal delivery systems (TDS) have been explored as an alternative over the oral route as they may avoid first-pass metabolism and intestinal degradation. As a TDS, microneedles (MN) have gained attention due to its easy to administration and painless. Furthermore, they are able to incorporate both free drug and nanoparticles, providing a modulated drug release (1). Nevirapine (NVP), is an antiretroviral drug used in the HIV treatment that belongs to the class of non-nucleoside reverse transcriptase inhibitors. Recently, the delivery of NVP in phthalated angico gum nanoparticles was reported as a relevant strategy to overcome NVP limitations (2). The objective of this work was to evaluate the influence of the incorporation of angico gum nanoparticles containing nevirapine (NP) in MN and to evaluate the NVP transdermal permeation from this device. Different volumes (2, 3 or 4 mL) of suspended nanoparticles (NPns) or lyophilized nanoparticles (NPfd) were incorporated into chitosan (CH) and polyvinylpyrrolidone (PVP) (5:3) hydrogel to produce MN (M-NPns and M- NPfd). The MN were produced by the micromolding method with a siloxane mold (needle with a pyramidal base; diameter: 200 µm; height: 800 µm). The selected M-NPns and M-NPfd were characterized by Scanning Electron Microscopy (SEM), permeation assays using Franz diffusion cell and pig ear as membrane;and histological studies using MN with 0.1% rhodamine. It was observed that both M-NPNs and M-NPfd provided significant drug permeation during 72 h of assay. In addition, histological assays showed that MN was able to promote micropierce in the skin. It was evidenced that the potential of NP application in CH:PVP-MN which presented suitable mechanical properties presenting a slow and progressive release of NVP.

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References

1. de Oliveira, T. C., Tavares, M. E. V., Soares-Sobrinho, J. L., & Chaves, L. L. (2022). The role of nanocarriers for transdermal application targeted to lymphatic drug delivery: Opportunities and challenges. *Journal of Drug Delivery Science and Technology*, 103110. Doi: 10.1016/j.jddst.2022.103110

2. de Oliveira, T. C., Oliveira, A. C. J., Patriota, Y. B. G., Chaves, L. L., Ribeiro, F. O. S., de Paula, R. C. M., . . . Soares-Sobrinho, J. L. (2021). Eco-friendly synthesis of phthalate angico gum towards nanoparticles engineering using Quality by Design (QbD) approach. *International Journal of Biological Macromolecules*, 190, 801-809. Doi: 10.1016/j.ijbiomac.2021.09.012

FC5

New approaches in the treatment and management of rosacea: a review

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Rosacea is a chronic and inflammatory skin disease, characterized by flushing, nontransient erythema, papules/pustules, telangiectasia, and phymatous changes. Secondary manifestations, such as itching, burning, or stinging, are often observed in patients with rosacea (1). The complex and multifactorial pathophysiology of rosacea requires an appropriate care plan covering three main aspects: pharmacological treatment, patient education and dermocosmetic care. Nevertheless, as rosacea is an incurable disease, new research is emerging to potentiate conventional formulations.

The aim of the present work is to highlight one of the current techniques widely developed for the treatment of rosacea: nanotechnology.

For the treatment of rosacea symptoms, nanotechnology mainly involves the use of lipid nanoparticles (namely nanostructured lipid carriers), nanoemulsions, liposomes, nanocrystals, and gold nanoparticles, where compounds such as metronidazole, azelaic acid, dapsone, and pioglitazone were loaded. Those substances are widely used in the treatment of rosacea as they have a high anti-inflammatory and antibacterial potential for the reduction of the symptoms. The nanosystems where these compounds were incorporated were characterized and it can be foreseen that their successful clinical application may improve the conventional treatments in terms of safety, efficacy, and stability.

As these nanosystems are capable of penetrating deeper layers of the skin, they may promote the controlled delivery of drugs and potentiate the effects of the active substances. Thus, these data are encouraging for upgrading the treatment of rosacea.

References

1. Zhang, H., Tang, K., Wang, Y., Fang, R., & Sun, Q. (2021). Rosacea Treatment: Review and Update. *Dermatology and therapy*, *11*(1), 13–24. Doi: 10.1007/s13555-020-00461-0

FC6

Optimization of Ibuprofen-loaded Transfersomes for Transcutaneous Delivery

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Ibuprofen oral formulations have been worldwide utilized for treatment of fever and pain. (1) However, there are several drug safety issues that pose in risk their therapeutic viability in special for chronic use. Transdermal delivery has been suggested as an interesting alternative but has a limited use because of the skin barrier. (2) To address this problem, nanodelivery systems appear as a useful tool. Therefore, the main goal of this work was to develop and optimize a transfersomal formulation made of mixed edge activators for the transdermal delivery of ibuprofen, using a Box-Behnken design (BBD) strategy. First, a 15-run BBD was performed to evaluate the influence of lipid concentration, edge activators ratio, and ibuprofen concentration in transfersomal properties (size, polydispersity index, PDI, zeta potential, ZP, encapsulation efficiency, EE, and loading capacity, LC). The nanosystems were produced by the thin film hydration method followed by sonication and characterized, as previously described. (3) In line with BBD predictions, the optimized transfersomal formulation showed encouraging properties: *ca.* 160 nm (size), <0.25 (PDI), <-40 mV (ZP), *ca.* 30% (EE) and 1% (LC), validating the experimental design used. Additionally, the impact of the transfersomes on the cell viability of 3D HaCaT cell cultures was assessed. The results showed that transfersomes, in the absence or presence of ibuprofen, did not reduce cell viability. Finally, transfersomal formulations were stable for two months under refrigerated storage, showing the potential of the optimized nanosystems for transdermal delivery.

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References:

1. Irvine, J., Afrose, A., & Islam, N. (2018). Formulation and delivery strategies of ibuprofen: challenges and opportunities. *Drug Development and Industrial Pharmacy*, *44*(2), 173–183. Doi:10.1080/03639045.2017.1391838

2. Júlio, A., Costa, J. G., Pereira-Leite, C., & Santos de Almeida, T. (2021). TransfersomILs: From Ionic Liquids toa New Class of Nanovesicular Systems. *Nanomaterials*, *12*(1), 7. Doi:10.3390/nano12010007

3. Witika, B. A., Mweetwa, L. L., Tshiamo, K. O., Edler, K., Matafwali, S. K., Ntemi, P. v, Chikukwa, M. T. R., & Makoni, P. A. (2021). Vesicular drug delivery for the treatment of topical disorders: current and future perspectives. *Journal of Pharmacy and Pharmacology*, *73*(11), 1427–1441. Doi:10.1093/jpp/rgab082

FC7

Comparative effect on the skin hydration at different hyaluronic acid delivery systems

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The microneedles (MNs) are being used as vehicles to deliver anti-aging cosmeceuticals molecules across the skin (1). In these applications, hyaluronic acid (HA) has been widely used as matrix material, because it is easy to fabricate into the microneedle and a naturally occurring substance in the human body. HA is an endogenous component of the extracellular matrix, with collagen and elastin. It decreases in the skin upon aging and is critical for tissue rejuvenation (2, 3). In this context, the aim of this study was to compare the *in vivo* skin hydration between two different delivery systems: the application of a HA microneedle patch; and a traditional AH hydrophilic gel. Skin hydration was quantified through the measurement of the capacitance of a dielectric medium. The data were collected at the following time points: baseline (T0), and 5, 30, 60, 120 and 180 minutes after the application. Results showed that both systems have the ability to hydrate the skin, however the HA MNs patch obtained a higher hydration value after 30 minutes after of the application. These findings suggest that MNs are one of the most promising technologies amongst the HA delivery methods.

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References

1. Han, T., & Das, D. B. (2015). Potential of combined ultrasound and microneedles for enhanced transdermal drug permeation: a review. *European Journal of Pharmaceutics and Biopharmaceutics*, 89, 312-328. doi:10.1016/j.ejpb.2014.12.020

2. Papakonstantinou, E., Roth, M., & Karakiulakis, G. (2012). Hyaluronic acid: A key molecule in skin aging. *Dermatoendocrinol*, 4(3), 253-258. doi:10.4161/derm.21923

3. Brown, M. B., & Jones, S. A. (2005). Hyaluronic acid: a unique topical vehicle for the localized delivery of drugs to the skin. *J Eur Acad Dermatol Venereol*, 19(3), 308-318. doi:10.1111/j.1468-3083.2004.01180.x.

FC8

Quercetin-loaded lipid nanoparticles with improved antioxidant capacity potential for skin applications

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Abstract content removed at the request of the authors

FC9

Application of placket-burman design in the development of phthalated Angico gum nanoparticles loaded with nevirapine

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Nanoparticles are a promising way to develop delivery systems applicable to the treatment of HIV. Among the various effective materials to produce nanoparticles, the use of polysaccharides that can be modified and used for application in drug delivery systems is expanding. Angico gum (AG), a polysaccharide from the exudation of the species *Anadenanthera colubrina var. cebil* is an example of this type. Despite presenting interesting properties, AG has hydrophilic chains that make its application difficult for the development of drug delivery systems. Chemical modification with phthalic anhydride has emerged as a strategy to overcome this limitation, since it introduces hydrophobic groups into the molecule by esterification. This work aimed to design phtalated AG (PAG)-based nanoparticles to encapsulate nevirapine (NVP) using a Plackett-Burman design to understand the influence of several factors in nanoparticles production. PAG proved to be a versatile material for producing nanoparticles with different characteristics. Optimized nanoparticles were produced using desirability parameters. NVP-loaded PAG nanoparticles formulation showed 202.1 nm of particle size, 0.23 of PDI, -17.1 of zeta potential, 69.8 of encapsulation efficiency, and promoted modified drug release for 8 h. Here we show that PAG presents as a promising biopolymer for drug delivery systems.

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References

1. de Oliveira, T. C., *et al.* (2021). Eco-friendly synthesis of phthalate angico gum towards nanoparticles engineering using Quality by Design (QbD) approach. *International Journal of Biological Macromolecules*, 190, 801-809. doi.org/10.1016/j.ijbiomac.2021.09.012

FC10

Evaluation of the photoprotective potential of *Schinus terebinthifolia raddi* (rose pepper) in cosmetic formulation

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Rose peper (*Schinus terebinthifolia raddi*) is a plant used in culinary and it have been investigated for pharmacological purposes and, photoprotective potential. Despite the ultraviolet (UV) exposure on human skin has positive effect, such as vitamin D synthesis, it's also responsible for premature skin aging, photosensitizing diseases and contribute to the increased incidence of skin cancer (1, 2). The aims of this work were to develop an emulsion containing the red pepper extract, and to evaluate the in vitro sun protection factor and its preliminary stability. The sunscreen formula (emulsion system) was composed by Crodafos® CES 6%, Optphen® 1%, hydroalcoholic extract 10% (with seed 10%, Herbal Foods®), tetrasodium EDTA 0,1%, glycerin 5%, and purified water (vehicle). The sample, in triplicate, was stored under the dark. The preliminary stability study was evaluated by cycles (24 hours at 45 ± 20 °C; 24 hours at -5 ± 20 C) for 12 days (6 cycles), following 3000 rpm at 30 min centrifuge. The organoleptic (appearance, colour and odour) and physicochemical (pH) characteristics were analysed. The sun protection factor (SPF) *in vitro* was evaluated by diffuse reflectance spectrophotometry with integration sphere (3). The sample showed a slight change in the color after the preliminary stability test, its aspect and odor remained the same and there was no pH variation outside the expected range (5.5 - 6.5), as well as no separation phases, after centrifuge. The cream with rose pepper and cream without extract were both SPF 1 ± 0,1, while the extract commercial hydroalcoholic extract showed SPF 2 ± 0,1. Although previous studies (based on the spectrophotometry UV absorbance at specific wavelengths) have suggested a photoprotection potential for the 10% extract, under the conditions of this study, this was not observed, the data of the cream and the extract SPF in vitro were low in the assay conditions.

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References

1. Furukawa, J. Y., Martinez, R. M., Morocho-Jácome, A. L., Castillo-Gómez, T. S., Pereda-Contreras, V. J., Rosado, C., . . . Baby, A. R. (2021). Skin impacts from exposure to ultraviolet, visible, infrared, and artificial lights - a review. J Cosmet Laser Ther, 23(1-2), 1-7. doi:10.1080/14764172.2021.1950767

2. Machado, B. C. T., Valentini, S. A. (2014). Avaliação do potencial farmacotécnico e antimicrobiano de diferentes extratos da aroeira pimenteira (Schinus terebenthifolius Raddi). *aBios-Revista Saúde e Biol* 1, 34-42.

3. COLIPA (2011). In Vitro Method for the determination of the UVA Protection Factor and "Critical Wavelength" values of Sunscreen Products. European Cosmetic, Toletry and Perfumery Association.

FC11

Antioxidant Essential Oils as Innovative Ingredients in Facial Masks

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The use of aromatic plants is well known since ancient times for their preservative and medicinal properties. Nevertheless, recently a renewed interest has arisen in the application of these materials in cosmetic products. Essential oils (E.O.) are complex mixtures of products obtained from aromatic plants consisting of various components with hydrophobic characteristics and high volatility, that make them unique. *Lavandula angustifolia* (Lavender), belonging to *Lamiaceae* family, *Spirostachys africana* Sond. (African sandal wood) from the *Euphorbiaceae* (2) family, *Chrysopogon zizanioides* (Vetiver) from *Poaceae* (3) family and *Corymbia citriodora* (Hook.) (Eucalytus citriodora) from the *Myrtaceae* family, have been traditionally used due to their antibacterial, antifungal, anticandidal, antioxidant, analgesic, and anti-inflammatory activities (4). These properties seem to indicate that the E.O. from these plants can provide beneficial effects when incorporated in skin formulations. The aim of this work was to probe the viability of gelatin-based films impregnated with E.O., which may be used as facial masks.

In this study, the antioxidant activity (A.A) of the E.O. was evaluated by the DPPH method. The results showed high A.A., after 24 hours, for all the E.O. studied (A.A. of 80 % - 83 %). Gelatin-based films bearing the E.O. were prepared. An optimization of the composition of the films with different concentrations of E.O., as well as variable proportions of water and ethanol was performed. The results showed that when the amount of water and ethanol decreased, the texture and flexibility of the films changed consequently. On the other hand, when the concentration of E.O. is higher two phases are formed, decreasing the flexibility of the film. An optimal flexibility and texture of the films was achieved, and further studies are ongoing for the application of these results on antioxidant E.O. impregnated masks.

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References

1. Edris, A. E. (2007). Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. *Phytother Res*, 21(4), 308-323. doi:10.1002/ptr.2072.

2. Mathabe, M. C., *et al.* (2008). Antibacterial activities and cytotoxicity of terpenoids isolated from Spirostachys africana. *J Ethnopharmacol,* 116(1), 194-197. doi:10.1016/j.jep.2007.11.017

3. Grover, M., *et al.* (2021). Chrysopogon zizanioides-a review on its pharmacognosy, chemical composition and pharmacological activities. *Environ Sci Pollut Res Int*, 28(33), 44667-44692. doi:10.1007/s11356-021-15145-1

4. Salem, M. Z. M., *et al.* (2018). Bioactivity of essential oils extracted from Cupressus macrocarpa branchlets and Corymbia citriodora leaves grown in Egypt. *BMC Complement Altern Med*, 18(1), 23. doi:10.1186/s12906-018-2085-0

Poster communications

P1

Self-assembly nanoparticles of bioactive compounds isolated from *Plectranthus spp.*

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The *Plectranthus* genus (Lamiaceae*)* consists of approximately 350 species, distributed globally, from Africa to Asia and Australia. Renowned for their medicinal properties, *Plectranthus* spp. are rich in diterpenoids, including different types of abietanes, widely used to treat different ailments, including cancer (1-3). Cytotoxic diterpenoids are often poorly water-soluble and nanotechnology can be a possible solution to improve drug solubility and targeted delivery, with minimized adverse effects. Previously, 7α-acetoxy6β-hydroxyroyleanone (4-5), obtained by fractionation of *P. hadiensis*, was employed as a starting material for the synthesis of self-assembled squalene nanoparticles. From *P. mutabilis* Codd., cytotoxic coleon U-quinone has demonstrated its potential as a lead compound for the preparation of nanosystems. In this study, we describe the isolation of coleon U-quinone from *P. mutabilis* for the development of derivatives as oleic acid-based nanoparticles. Overall, we expect that nanoparticle delivery systems, besides improving drug solubility and stability, may extend a better therapeutic action of these abietane analogues.

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References

1. Ladeiras, D., Monteiro, C. M., Pereira, F., Reis, C. P., Afonso, C. A., Rijo, P. (2016). *Curr Pharm Des* 22, 1682-714. Doi: 10.2174/1381612822666151211094521
2. Matias, D., Nicolai, M., Saraiva, L., Pinheiro, R., Faustino, C., Diaz Lanza, A., *et al*. (2019). *ACS Omega* 4, 8094–103. Doi: 10.1021/acsomega.9b00512
3. Garcia, C., Teodosio, C., Oliveira, C., Oliveira, C., Diaz-Lanza, A., Reis, C., *et al.* (2018). *Curr Pharm Des* 24, 4207-36. Doi: 10.2174/1381612825666190115144241
4. Bernardes, C. E. S., Garcia, C., Pereira, F., Mota, J., Pereira, P., Cebola, M. J., *et al.* (2018). *Mol Pharm* 15, 1412-9. Doi: 10.1021/acs.molpharmaceut.7b00892
5. Sitarek, P., Toma, M., Ntungwe, E., Kowalczyk, T., Skała, E., Wieczfinska, J., *et al*. (2020). *Biomolecules*. 10(2), 194. Doi: 10.3390/biom10020194

P2

Medicinal Centauri Honey: a Innovative Ingredient?

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Honey is a natural product that has been used over the centuries as a medicine due to its antioxidant and antimicrobial properties. This natural product is mainly composed of a supersaturated solution of sugars (namely fructose and glucose) with a low water content and minor concentrations of bioactive compounds. The honeybees (*Apis mellifera*) produce honey from the nectar of flowers. The flower source, climate, geographical origin, harvesting process and storage conditions are factors that influence the composition of the nectar, leading to significant changes in the chemical composition, physical properties and bioactivity of honey (1). Centauri Honey is cultivating high up in the hills of Turkey by a bee's colony from wild alps in the mountains 2,500 meters above the Black Sea. The bees live in caves far from human settlements and other bees, a guarantee against the scourge of parasites such as varroa destructor, normally eradicated by pesticides. They have access to medicinal endemic blooms throughout the year. Drug Administration Center Benzialem University described the chemical constituents of Centauri honey, by a LC-HRMS method, resulting in a very rich composition of flavonoids, chrysin, salicylic acid and polyphenols. The Scientific and Technical Research Council of Turkey analyzed the Centauri honey samples and determined the total phenol analysis (77.65 mg gallic acid equivalent/100g), the total flavonoids quantification (18.53 mg quercetin equivalent/100g) and the total antioxidant activity (74.75 mg Trolox equivalent/100g).

Further studies will be conducted to assess the antimicrobial and anticancer effects to scientifically validate the medicinal properties of Centauri Honey due to its exceptional chemical composition and thus become an Innovative Ingredient.

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References

1. Gonçalves, J., Ribeiro, I., Marçalo, J., Rijo, P., Faustino, C., Pinheiro, L. (2018). Physicochemical, Antioxidant and Antimicrobial Properties of selected Portuguese Commercial Monofloral Honeys. *J Food Nutr Res* 6(10), 645-654. doi:10.12691/jfnr-6-10-5

P3

Polyurea (PURE) dendrimers as modulators of membrane permeability to enhance cisplatin delivery

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Cisplatin is a widely used anti-cancer drug that cross-links with DNA. Its stability and permeability are susceptible to a variety of factors including pH and osmolality that result in an equilibrium of "aquated" species with different physicochemical properties. Growing evidence also suggests lipids have an important role in the mechanism of resistance of cells to cisplatin (1). To overcome these issues, dendrimers are a class of polymers with high potential for drug delivery applications due to their precise size and cationic surface properties that interact with cellular membranes. Moreover, modified PURE dendrimers showed the capacity to increase the sensitivity of cells to carboplatin (2). Herein, we explored the potential of PURE dendrimers to interact with different lipid model membranes to understand their effect on permeability enhancement using a leakage assay. The results showed that dendrimers were able to alter the membrane permeability that was dependent on both their size and lipid composition. Overall, this provides a proof-of-concept of using dendrimers to increase the permeability of membranes to overcome cisplatin resistance limited by membrane lipid composition.

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References

1. Martinho, N., Santos, T. C. B., Florindo, H. F., Silva, L. C. (2019). Cisplatin-Membrane Interactions and Their Influence on Platinum Complexes Activity and Toxicity. *Frontiers in Physiology,* 9, 1898. doi: 10.3389/fphys.2018.01898
2. Cruz, A., Mota, P., Ramos, C., Pires, R. F., Mendes, C., Silva, J. P., Nunes, S. C., Bonifácio, V. D. B., Serpa, J. (2020). Polyurea Dendrimer Folate-Targeted Nanodelivery of L-Buthionine Sulfoximine as a Tool to Tackle Ovarian Cancer Chemoresistance. *Antioxidants*, 9(2), 133. doi: 10.3390/antiox9020133

P4

Bovine Milk Exosomes: A Comparative Study of Different Isolation Methods

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Milk is a well-known and widely consumed natural delivery system. In its constitution, besides carbohydrates, proteins, lipids, and minerals, it is also possible to find extracellular vesicles, called exosomes (Exo) (1). Several studies have been showing their potential as delivery systems for a variety of compounds and applications (2). However, a more extensive application of Exo for drug delivery is still dependent on the development of more efficient, safer, and cost-effective extraction processes. Thus, in this work, different isolation methods were tested on raw bovine milk, aiming to achieve a good trade-off between yield and purity of the final exosomal suspensions. The tested methods involved an initial casein extraction (by casein chelation adding EDTA, acid precipitation with acetic acid, or a combination of both) followed by ultracentrifugation. Exosomal suspensions were characterized by dynamic light scattering (DLS), nanoparticle tracking analysis (NTA), and bicinchoninic acid assay (BCA). DLS and NTA size measurements showed a non-unimodal distribution, characteristic of natural occurring nanovesicles. The method that resulted in the highest yield and purity was the EDTA-based method, resulting in an exosomal suspension with 1.45×10^9 Exo/µg protein, and a yield of 4.11×10^{10} Exo/ml of milk. Also, by comparing the size exclusion chromatograms between the exosomal suspensions and whey, the EDTA-based method resulted in a chromatogram with only one peak in a region corresponding to the Exo, indicating low contamination by other milk proteins.

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References

1. Zempleni, J., Sukreet, S., Zhou, F., Wu, D., & Mutai, E. (2019). Milk-derived exosomes and metabolic regulation. *Annual review of animal biosciences*, 7, 245-262. doi: 10.1146/annurev-animal-020518-115300

2. Ngu, A., Wang, S., Wang, H., Khanam, A., & Zempleni, J. (2022). Milk exosomes in nutrition and drug delivery. *American Journal of Physiology-Cell Physiology*, 322(5), C865-C874. doi: 10.1152/ajpcell.00029.2022

P5

A systematic review of the emerging 5-fluorouracil nanotheranostic agents for cancer treatment

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P6

Development of lipid nanoparticles based on fatty acids to promote healthy skin regeneration

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It is estimated that 2 million Europeans suffer from acute or chronic skin lesions, greatly affecting their quality of life. Skin lesions are the result of the disruption of skin's functional structure which lead to an increase in transepidermal water loss, the incidence of infections, as well as scarring.

Thus, the main objective of this work was to develop solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), consisting of a mixture of fatty acids to act as emollients, and to deliver 3-aminopropionitrile fumarate (BAPN), to avoid excessive scaring during skin lesion regeneration. The physicochemical properties of SLN and NLC as well as their accelerated and long-term stability were evaluated. At last, the *in vivo* skin compatibility of the unloaded nanoparticles was assessed by patch test and their efficacy was assessed by the tape striping technique.

The in vitro results showed that the type and composition of nanoparticles influence their physicochemical properties. Both SLN and NLC displayed promising diameters for cutaneous administration, with NLC having a slightly smaller diameter. Considering the in vivo results, after 24 h in contact with the skin, a good biocompatibility was observed for both nanoparticles. Additionally, the erythema after tape striping was reduced in the sites treated with both nanoformulations.

According to these preliminary results, the development of lipid nanoparticles based on fatty acids has shown potential to facilitate the regeneration of skin lesions and to be a proper vehicle to deliver skin scaring modulators.

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P7

Chitin-Glucan Complex Hydrogels: Optimization of Gel Formation and Demonstration of Drug Loading and Release Ability

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The human skin provides a unique delivery pathway for therapeutic and other active agents. Drug release to the skin is commonly accomplished by the use of transdermal systems that allow topical delivery to the skin or transdermal delivery into the systemic circulation. Transdermal drug delivery is an important area of biomedicine, wherein intensive research is carried out for the development of novel advanced systems. Although several approaches have been proposed and implemented, including the use of synthetic and natural polymers to produce hydrogels, there is a continued interest in the search for alternative biomaterials suitable for the development of transdermal delivery systems with new or improved properties. In view of this, microbial polysaccharides, such as chitin-glucan complex (CGC), are valuable candidates for the development of novel biomaterials. The gel-forming capacity of this biopolymer was recently demonstrated (1), and thus, the aim of this study was the optimization of gel formation and demonstration of drug loading and release ability.

CGC hydrogels were fabricated through a freeze-thaw procedure for biopolymer dissolution in NaOH 5 mol/L, followed by a dialysis step to promote gelation. Compared to a previously reported methodology that included four freeze-thaw cycles, reducing the number of cycles to one had no significant impact on the hydrogels' formation, as well as reducing the total freezing time from 48 to 18 h. The optimized CGC hydrogels exhibited a high and nearly spontaneous swelling ratio (2528 ± 68%) and a water retention capacity of 55 ± 3%, after 2 h incubation in water, at 37 ◦C. Upon loading with caffeine as a model drug, an enhancement of the mechanical and rheological properties of the hydrogels was achieved. In particular, the compressive modulus was improved from 23.0 ± 0.89 to 120.0 ± 61.64 kPa and the storage modulus increased from 149.9 ± 9.8 to 315.0 ± 76.7 kPa. Although the release profile of caffeine was similar in PBS and NaCl 0.9% solutions, the release rate was influenced by the solutions' pH and ionic strength, being faster in the NaCl solution. These results highlight the potential of CGC based hydrogels as promising structures to be used as drug delivery devices in biomedical applications.

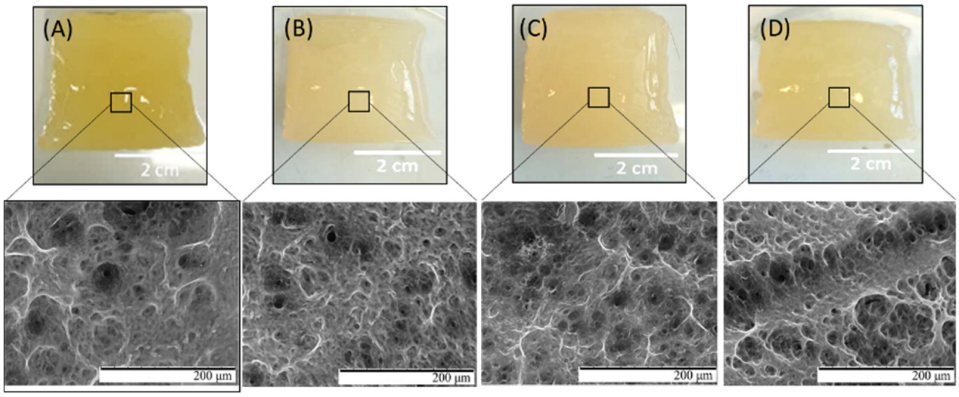

Figure 1 – Macroscopic aspect and SEM images of CGC hydrogels with (A) 1, (B) 2, (C) 3 freeze-thawing cycles with 48 h freezing and (D) 1 freeze-thawing cycle with 18 h freezing, under magnification 500 ×.

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References

1. Araújo, D., Alves, V. D., Lima, S. A. C., Reis, S., Freitas, F., & Reis, M. A. M. (2020). Novel hydrogels based on yeast chitin-glucan complex: Characterization and safety assessment. *Int J Biol Macromol*, 156, 1104-1111. doi:10.1016/j.ijbiomac.2019.11.141

P8

Antioxidants from agro-industrial waste: valorisation for the cosmetic industry

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P9

O/W emulsions containing glycinate-based ILs and phenolic compounds

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In the last years, phenolic compounds, one of the main classes of natural compounds, have shown relevant biological activities, such as antioxidant and anticancer. However, they show low aqueous solubility, which impairs their incorporation into delivery systems. This drawback may be overcome using ionic liquids (ILs), which have presented several valuable functionalities in the development of delivery systems (1).

With this in mind, this work studied the influence of three glycinate based ILs, (2-hydroxyethyl)trimethylammonium-L-glycinate [Cho][Gly], 1-ethyl-3-methylimidazolium glycinate [Emim][Gly], and 1-butyl-3-methylimidazolium glycinate [Bmim][Gly] on the incorporation of ferulic, caffeic or *p*-coumaric acids, or rutin into oil-in-water (O/W) emulsions. The ILs were incorporated in the formulations at the maximum concentration which allowed the viability of HaCaT cells to be maintained, and then their impact on the stability of the developed systems, was evaluated.

The ILs allowed a higher drug loading into the formulations, by enhancing the aqueous solubility of the bioactive compounds (between 2 and 3-fold). Additionally, the ILs also doubled the viscosity of the emulsions, which seemed to improve the stability over time and may be used tune the sensorial features of the developed emulsions.

Our work demonstrated that ILs may be useful to improve the performance and sensorial properties of the O/W emulsions, to be used in the pharmaceutical or cosmetic fields.

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References

1. Caparica, R., Júlio, A., Fernandes, F., Araújo, M.E.M., Costa, J.G., Santos de Almeida, T. (2021). Upgrading the Topical Delivery of Poorly Soluble Drugs Using Ionic Liquids as a Versatile Tool. *International Journal of Molecular Sciences,* 22, 4338. doi: 10.3390/ijms22094338

P10

Ionic and Aerogel Levothyroxine formulations for drug delivery

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Levothyroxine (T4) is used clinically to treat hypothyroidism, however, the narrow therapeutic index of this drug, the need for a frequent administration and the influence of gastrointestinal diseases, foods and other drugs on its absorption are the shortcomings related with oral administration of T4 (1, 2). There are several approaches to enhance the drug solubility and bioavailability such as particle size reduction, nanosuspension, use of surfactants, salt formation, solid dispersion, among others (3). In this work, an attempt to improve T4 solubility through the synthesis of T4 salts based on Organic Salts and Ionic Liquids (OSILs) and on its dispersion into biocompatible aerogels matrixes, is made. OSILs based on pharmaceutical drugs (API-OSILs) is a class of salts with promissory therapeutic properties (4). Herein, T4 was used as anion in combination with choline and 1ethanol-3-methylimidazolium [C2OHMIM] cations. All compounds were characterized by 1H- and 13C-NMR, FTIR and elemental analysis in order to confirm their structures and purity levels. Aerogels are a special class of nanoporous materials with growing application in the biomedical and pharmaceutical fields due to their open pore structure and high surface area capable of active adsorption and releasing desired compounds.[5] The use of polysaccharides for the synthesis of aerogel matrices has additional benefits such as biodegradability and biocompatibility, which make them, promising as encapsulation and delivery systems of drug (5). In this work, composite aerogels based on locust bean gum and k-carrageenan were used as T4 carriers and delivery studies performed allowing for the determination of the drug solubility. The water and serum solubility of the prepared T4-OSILs as well as the thermal analysis through differential scanning calorimetry (DSC) studies, have been carried out and also compared with original T4 drug. The poor watersoluble pharmaceutical drug T4 was loaded into the aerogel matrixes and the composites were characterized by attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) and by DSC; the results were compared with the original T4 drug. Release experiments were performed at physiologic pH using a phosphate buffer solution at pH 7.2.

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References:

1. Chiovato, L., Magri, F., & Carlé, A. (2019). Hypothyroidism in Context: Where We've Been and Where We're Going. *Adv Ther*, 36(Suppl 2), 47-58. doi:10.1007/s12325-019-01080-8
2. Wartofsky, L. (2002). Levothyroxine: therapeutic use and regulatory issues related to bioequivalence. Expert Opin Pharmacother, 3(6), 727-732. doi:10.1517/14656566.3.6.727
3. Patel, V. R., & Agrawal, Y. K. (2011). Nanosuspension: An approach to enhance solubility of drugs. J Adv Pharm Technol Res, 2(2), 81-87. doi:10.4103/2231-4040.82950.
4. a) Marrucho, I. M., Branco, L. C., & Rebelo, L. P. (2014). Ionic liquids in pharmaceutical applications. Annu Rev Chem Biomol Eng, 5, 527-546. doi:10.1146/annurev-chembioeng-060713-040024. b) Ferraz, R., Silva, D., Dias, A. R., Dias, V., Santos, M. M., Pinheiro, L., . . . Branco, L. C. (2020). Synthesis and Antibacterial Activity of Ionic Liquids and Organic Salts Based on Penicillin G and Amoxicillin hydrolysate Derivatives against Resistant Bacteria. Pharmaceutics, 12(3), 221. doi:10.3390/pharmaceutics12030221
5. Hiremath, C., Heggannavar, G. B., Mitchell, G. R., Kariduraganavar, M. Y. (2016). Biopolymers in Drug Delivery Applications In Inamuddin, (Ed.). Green Polymer Composites Technology: Properties and Applications (1st ed.). CRC Press. https://doi.org/10.1201/9781315371184

P11

Impact of the loaded phytochemical on TransfersomILs performance

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TransfersomILs, i.e., transfersomes containing ionic liquids (ILs), were recently developed within our group and ILs were found to modulate the size, association efficiency, drug release, and colloidal stability of these nanovesicular systems (1). These nanocarriers are particularly relevant for cutaneous applications, particularly for the delivery of phytochemicals with antioxidant and anti-inflammatory properties.
Thus, this study aimed to evaluate the impact of loading rutin or ferulic acid on the performance of TransfersomILs made of imidazole- and cholinium-based ILs, concerning their physicochemical properties and colloidal stability under refrigerated conditions.
Various physicochemical properties of the TransfersomILs were dependent on the type of phytochemical incorporated, namely, vesicle size, polydispersity index, potential zeta, association efficiency (AE), and loading capacity (LC). Despite that fact, the incorporation of ILs in transfersomes, to load both phytochemicals, appears to decrease the vesicle size and improve the AE, LC, and storage stability of these nanodelivery systems. Therefore, TransfersomILs seem to be valuable nanocarriers to boost the skin delivery of phytochemicals for pharmaceutical and/or cosmetic applications.

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References

1. Júlio, A., Costa, J. G., Pereira-Leite, C., Santos de Almeida, T. (2022). TransfersomILs: From Ionic Liquids to a New Class of Nanovesicular Systems. *Nanomaterials*, 12, 7. doi: 10.3390/nano12010007

P12

Advanced natural formulations to tackle skin ageing

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In the last years, the skin care industry has been focused on searching for new active compounds to prevent and retard skin ageing. Dehydroabietic acid (DHA) is a phytochemical found in red pine trees and herbal plants (1), and some studies suggest that DHA has anti-inflammatory effects on macrophages and regenerative effects in human dermal fibroblasts (1, 2). This work aimed at developing semi-solid formulations containing solid lipid nanoparticles (SLN) to encapsulate DHA, as a possible strategy for skin delivery. After preparation, SLN control (without DHA) and loading DHA were characterized in terms of size, polydispersity index (PDI), and zeta potential (ZP). Then, these nanoparticles were incorporated in an alginate hydrogel and the gel's stability, in terms of pH and viscosity, was evaluated for 30 days. The results indicate that the developed SLN presented satisfactory characteristics for skin applications with sizes varying between 145-170 nm, PDI lower than 0.2, and ZP values around -20 mV. The pH of the produced gels was around 5.0 (compatible with the skin) and viscosity was maintained above 15,000 mPa.s, remaining reasonably stable throughout 30 days. Our results suggest that the development of DHA-loaded SLN in hydrogels could be a useful delivery strategy for preventing skin photoaging.

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References

1. Park, N., Kang, Y., Kim, S., Bae, I., Lee, S., & Kim, D. et al. (2019). Dehydroabietic Acid Induces Regeneration of Collagen Fibers in Ultraviolet B-Irradiated Human Dermal Fibroblasts and Skin Equivalents. *Skin Pharmacology and Physiology*, 32(2), 109-116. doi: 10.1159/000497103.

2. Kang, M., Hirai, S., Goto, T., Kuroyanagi, K., Lee, J., & Uemura, T. et al. (2008). Dehydroabietic acid, a phytochemical, acts as ligand for PPARs in macrophages and adipocytes to regulate inflammation. *Biochemical And Biophysical Research Communications*, 369(2), 333-338. doi:10.1016/j.bbrc.2008.02.002

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