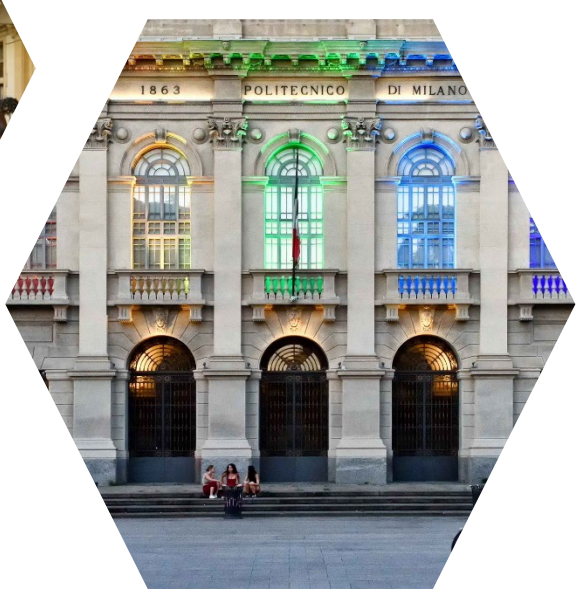
EuroCD 2025

8th European Cyclodextrin Conference



Book of Abstracts

9th-12th September 2025

Politecnico di Milano

EuroCD 2025 - 8th European Cyclodextrin Conference

Politecnico di Milano, 9th-12th September 2025

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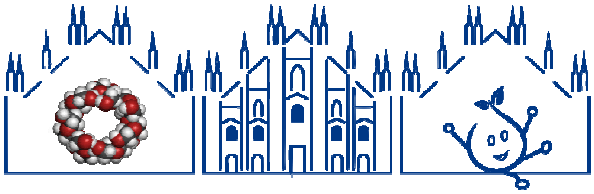

EuroCD 2025

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Detailed Day-by-day Schedule/Program

Tuesday 9th September

11:00 - 15:30	**Registration**	
15:30 - 16:00	**Opening** **Isabella Nova** - *Deputy rector* **Marinella Levi** - *Head of Department*	
16:00 - 16:40	**PL1**	**Frank Biedermann**
16:40 - 17:00	**KN1**	**Gjylije Hoti**
17:00 - 17:20	**OP1**	**Marco Agnes**
17:20 - 17:40	**OP2**	**Kasper S. Hedergaard**
17:40 - 18:00	**OP3**	**Sébastien Rigaud**
18:00 - 18:20	**OP4**	**Maddalena Sguizzato**
18:30 - 21:00	**Welcome cocktail**	

Wednesday 10th September

8:30 - 9:00	**Registration**	
9:00 - 9:40	**PL2**	**Andreas Bernkop-Schnürch**
9:40 - 10:00	**OP5**	**Antonino Mazzaglia**
10:00 - 10:20	**OP6**	**Vincent Dumouilla**
10:20 - 10:40	**OP7**	**Noemi Bognanni**
10:40 - 11:00	**Coffee**	
11:00 - 11:20	**KN2**	**Lucio Melone**
11:20 - 11:40	**OP8**	**Nicolas Tinet**
11:40 - 12:00	**OP9**	**Anita Kiss**
12:00 - 12:20	**OP10**	**Cristina Parisi**
12:20 - 12:40	**OP11**	**Mary McNamara**
12:40 - 13:00	**OP12**	**Daniel Ondo**
13:00 - 14:10	**Lunch**	
14:10 - 14:30	**OP13**	**Jindřich Jindřich**
14:30 - 14:50	**OP14**	**Saverio Aliberti**
14:50 - 15:10	**OP15**	**Milena Sorrenti**
15:10 - 15:30	**OP16**	**Yareli Rojas-Aguirr**
15:30 - 16:40	**Poster session + Coffee**	
16:40 - 18:00	**FP**	
18:30 - 21:00	**Guided tour**	

Thursday 11th September

9:00 - 9:40	**PL3**	**David H. Thompson**
9:40 - 10:00	**OP17**	**Francesca Laneri**
10:00 - 10:20	**OP18**	**François-Xavier Legrand**
10:20 - 10:40	**OP19**	**Ana-Maria Resmerita**
10:40 - 11:00	**Coffee**	
11:00 - 11:20	**OP20**	**Damien Truffin, Julien Parcq**
11:20 - 11:40	**OP21**	**Carmen Alvarez-Lorenzo**
11:40 - 12:00	**OP22**	**Elisabetta Lacolla**
12:00 - 12:20	**OP23**	**Sylvain Laclef**
12:20 - 12:40	**OP24**	**Adrian Matencio**
12:40 - 13:00	**OP25**	**Balazs Kondoros**
13:00 - 14:10	**Lunch**	
14:10 - 14:30	**KN3**	**Sophie Fourmentin**
14:30 - 14:50	**OP26**	**Giuseppe Nocito**
14:50 - 15:10	**OP27**	**Paolo Di Gianvincenzo**
15:10 - 15:30	**OP28**	**Yoshinori Takashima**
15:30 - 15:50	**OP29**	**Mariachiara Trapani**
15:50 - 17:00	**Poster session + Coffee**	
17:00 - 18:20	**FP**	
20:30 - 23:00	**Social dinner**	

Friday 12th September

9:00 - 9:40	**PL4**	**Ruxandra Gref**
9:40 - 10:00	**OP30**	**Daniel I. Hădărugă**
10:00 - 10:20	**OP31**	**Antonella Vitiello**
10:20 - 10:40	**OP32**	**Siddanth Saxena**
10:40 - 11:00	**Coffee**	
11:00 - 11:20	**KN4**	**Milo Malanga**
11:20 - 11:40	**OP33**	**Michal Řezanka**
11:40 - 12:00	**OP34**	**Askar Gatiatulin**
12:00 - 12:20	**OP35**	**Bettina Rávai**
12:20 - 12:40	**OP36**	**Angela Scala**
12:40 - 13:15	**1st T. Loftsson Award**	
13:15 - 13:30	**Concluding remarks**	

PL: Plenary Lecture
OP: Oral Presentation
KN: Keynote Presentation
FP: Flash Presentation

Plenary Lectures

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PL01

Challenges in the Determination of Binding Constants: The Role of Fitting Algorithms, Improved Assay Design, and Open-Access Solutions

Frank Biedermann, Ahmad Omira Konrad Krämer, Vahideh Mahram, and Nicole Jung

Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany.

Presenting author email: frank.biedermann@kit.edu

The determination of **binding constants** (K_a, K_d, ΔG) is fundamental to supramolecular host-guest chemistry and molecular recognition studies. However, we show that commonly used least-square fitting procedures can yield deceptively precise affinity values. In contrast, a comprehensive exploration of parameter space reveals that identical experimental binding isotherms can be fitted equally well by multiple parameter combinations, indicating that confidence intervals on binding constants are often largely underestimated. Our findings demonstrate that **fitting errors can easily surpass those of replicate measurements**, suggesting that traditional replication alone is insufficient to establish realistic error margins for affinity values. This has profound implications for the use of binding constants as system descriptors and may explain discrepancies in reported values for the same host–guest pairs across different laboratories.

To address these issues, we introduce **openly accessible R- and Python-based applications with graphical user interfaces**. Additionally, we present improvements in binding assay design, particularly in microplate reader experiments, with broader applicability to cuvette titrations [1,2].
Beyond methodological advancements, we highlight the latest developments in **SupraBank.org**, an open-access and FAIR repository for binding constants and related physicochemical parameters [3].
Finally, we introduce our **Reference Lab Initiative**, which provides independent validation of binding constants via optical and calorimetric methods—offered in-kind, without co-authorship requirements—to help address the reproducibility crisis in supramolecular chemistry.

[1] https://github.com/ASDSE
[2] https://github.com/ComPlat/Thermosimfit
[3] https://suprabank.org/

Biosketch:

P.D. Dr. Frank Biedermann is a supramolecular chemist specializing in chemosensor development. He earned his B.Sc. from Leipzig University in 2004 and subsequently completed his M.Sc. and Ph.D. at the University of Cambridge under Prof. Oren Scherman, focusing on supramolecular and polymer chemistry. Postdoctoral research followed at Jacobs University Bremen with Prof. Werner Nau and at the Institut de Science et d'Ingénierie Supramoléculaires in Strasbourg with Prof. Luisa De Cola, where he explored supramolecular analytical chemistry and metal-organic materials.
In 2016, Dr. Biedermann established an independent research group at the Karlsruhe Institute of Technology (KIT) through the prestigious Emmy Noether Grant from the German Research Foundation. His team specializes in developing advanced supramolecular chemosensors for applications in sensing, imaging, and molecular diagnostics. In recognition of his contributions, he received the Aventis Life Science Bridge Award in 2021. Since mid-2023, he leads a prestigious ERC Consolidator group at KIT, focusing on the development of "SupraSensors" for small molecule detection in biofluids. In 2024, he received his habilitation degree at the KIT.

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PL02

Thiolated Cyclodextrins in Drug Delivery

Andreas Bernkop-Schnürch[1]

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Cyclodextrins (CDs), with an external diameter of 1-2 nm, are considered the smallest nanocarriers in drug delivery. Due to their solubilizing and protective properties, they are widely used as excipients in many commercially available drug products. Recent studies have shown that thiolation can further expand their range of pharmaceutical applications. Thiolated cyclodextrins are created through hydroxyl-to-thiol substitutions or the covalent attachment of sulfhydryl groups to the oligomeric backbone of various types of CDs. The ability of thiolated CDs to form disulfide bonds with endogenous proteins, such as mucins, keratins, and cysteine-rich receptor proteins, opens up virtually limitless possibilities for pharmaceutical and medicinal applications [1,2]. Notably, their ability to form disulfide bonds with cysteine-rich subdomains of mucus glycoproteins has been shown to significantly enhance their mucoadhesive properties. Additionally, thiolated CDs exhibit other beneficial characteristics, such as in-situ gelling, efflux pump inhibition, permeation enhancement, and improved cellular uptake [3]. These enhanced properties pave the way for the development of a wide range of innovative drug delivery systems.

[1] G. Kali, S. Haddadzadegan, A. Bernkop-Schnürch *Carbohydr Polym*. (2024) 324, 121500.
[2] S. Noreen, A. Bernkop-Schnürch *Adv. Funct. Mat.* (2024) 34, 2310129.
[3] F. Veider, S. Haddadzadegan, E. Sanchez Armengol, F. Laffleur, G. Kali, A. Bernkop-Schnürch *Carbohydr Polym*. (2024) 327, 121648.

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PL03

Development of an agile nucleic acid delivery system using polycationic cyclodextrins and elastin-like polypeptides in a layer-by-layer approach

Aayush Aayush, Saloni Darji, Feng Qu, Joydeep Rakshit and David H. Thompson

Department of Chemistry, Purdue University, Multi-disciplinary Cancer Research Facility, Bindley Bioscience Center, 1203 W. State Street, West Lafayette, Indiana, 47907, United States

Presenting author email: davethom@purdue.edu

We report a versatile elastin-like polypeptide (ELP) carrier system using a layer-by-layer (LbL) formulation approach that delivers nucleic acid cargoes ranging in size from siRNA to plasmids. The ELP components are rapidly purified using an organic solvent extraction-precipitation method [1,2] that retains their biological activity [2,3]. The cyclodextrin components are prepared by coupling cationic polypeptides with β-cyclodextrin derivatives. The system can be reconfigured to modulate the biochemical and biophysical characteristics of the carrier to engage the unique features of the biological target. The physical characterization and biological performance of LbL ELP nucleic acid nanoparticles (LENN) in bladder tumor cells will be described [4].

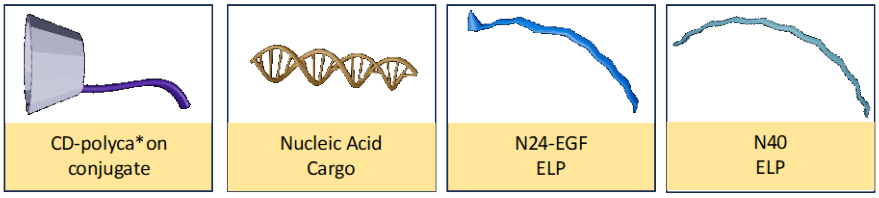

Figure 1. Conceptual diagram of LENN complexes formed.

Acknowledgements: Supported by the Purdue Institute for Cancer Research (P30 CA023168).

[1] C. Sweet, A. Aayush, L. Readnour, K. V. Solomon, D. H. Thompson, *Biomacromolecules* (2021) 22, 1990.
[2] Aayush, S. Darji, D. Dhawan, A. Enstrom, M. M. Broman, M. T. Idrees, H. Kaimakliotis, T. Ratliff, D. Knapp, D. H. Thompson, *Oncotarget* (2022) 13, 1004.
[3] S. Darji, A. Aayush, K. M. Estes, J. D. Strock, D. H. Thompson, *Biomacromolecules* (2024) 25, 272.
[4] Aayush, S. Darji, K. M. Estes, E. Yeh, D. H. Thompson, *Biomacromolecules* (2024**)** 25, 5729.

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PL04

Drug delivery systems based on cyclodextrins to treat severe infections

Ruxandra Gref

Université Paris-Saclay, CNRS, Institute of Molecular Sciences of Orsay, 91405 Orsay, France

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Despite medical advances, tuberculosis (TB) remains a leading cause of infectious mortality, with around 1.3 million deaths annually. Ethionamide (ETH), a key second-line anti-TB drug, is limited by severe side effects, poor water solubility, and a strong tendency to crystallize. “Booster” molecules have been developed to significantly enhance ETH efficacy, offering promising strategies for drug-resistant TB.

To enable co-delivery of ETH and booster to the lungs, both compounds were encapsulated in cyclodextrin-based polymers. This approach overcame solubility and crystallization challenges, significantly improving drug apparent solubilities in water. The drugs localized both in cyclodextrin cavities and within confined microdomains of the polymer network. This dual encapsulation mode, along with higher binding affinities, emphasizes the benefit of using polymers over monomeric cyclodextrins. Competitive binding studies showed no interference between the two drugs, validating their co-loading.

The formulations were tested in M. tuberculosis-infected macrophages. The most promising candidates were evaluated in a TB mouse model, where they were well tolerated and achieved a 3-log reduction in pulmonary bacterial load.

Notably, cyclodextrin-based polymers also showed intrinsic antibacterial activity, impairing TB establishment and creating a lung environment unfavorable to bacterial survival. This effect is linked to the polymers’ physicochemical properties.

Together, these results support the dual therapeutic potential of cyclodextrin polymers for future anti-TB regimens.

[1] J. Costa-Gouveia et al., *Scientific Reports.* (2017) 7: 5390.
[2] G. Salzano et al., *International Journal of Pharmaceutics,* (2017) 2, 577.
[3] A. Machelart et al., *ACS Nano,* (2019) 13, 3992.
[4] A. Pochet et al., *Carbohydrate Polymer Technologies and Applications,* (2025) 11, 100921.

Keynote Presentations

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KN01

Evaluation of Cross-Linking Density and Monomer Composition in Cyclodextrin-based Nanosponges Using a Multi-Technique Approach

Gjylije Hoti[1,2], Fabrizio Caldera[1], Monica Argenziano[2], Roberta Cavalli[2], and Francesco Trotta[1]

[1]Department of Chemistry, University of Turin, Via P. Giuria 7, Turin, 10125, Italy
[2]Department of Drug Science and Technology, University of Turin, Via P. Giuria 9, Turin, 10125, Italy

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Cyclodextrin-based nanosponges (CD-NSs) are cross-linked polymer networks synthesized by cross-linking cyclodextrins (CDs) with appropriate agents, whose swelling behavior and hydrogel-forming capability in aqueous media are directly influenced by their cross-linking density. While the degree of cross-linking is a critical feature of this polymer network, particularly for the application of CD-based NSs in drug delivery, yet its determination remains highly challenging [1-4].
This study investigates the crosslinking density (υ) and the molecular weight between crosslinking points (M_c) of β-cyclodextrin-based nanosponges synthesized by esterification with varying pyromellitic anhydride (PMDA) amounts (2–10 mol per mol of β-CD), as a cross-linking agent, using a one-step synthesis. Flory-Rehner's swelling theory and rheology, with water absorption capacity (WAC) as a key parameter, revealed that the cross-linking process allows for the modulation of the swelling and mechanical stability of the nanocarriers. The synthesized CD-NSs exhibit a response to the acidic pH of the gastrointestinal (GI) tract due to the presence of carboxylic groups and exhibit strong mucoadhesive properties (80.0-94.5%), which can be attributed to the saccharide nature of the polymer. Additionally, thermogravimetric and elemental analyses (TGA and EA) were used to experimentally determine the monomer reactivity ratio. Potentiometric titration and zeta potential analyses were further employed to characterize the PMDA/β-CD ratio and the balance between ester linkages and free carboxylic groups, confirming the influence of cross-linking agent content on the polymeric network structure. Comparison of theoretical and experimental values offered insights into the synthesis efficiency and structure-property relationships of CD-NSs. Understanding the reactivity of CDs with cross-linking agents is crucial for designing tailored materials and broadening the industrial applications of CD-NSs.

Acknowledgements: The research activity of Gjylije Hoti is part of the NODES project, which has received funding from the MUR–M4C2 1.5 of PNRR with the grant agreement no. ECS00000036. Authors acknowledge support from the Project CH4.0 under the MUR program "Dipartimenti di Eccellenza 2023-2027" (CUP: D13C22003520001). β-CD is kindly gifted by Roquette Freres (Lestrem, France).

[1] H. Gjylije, C. Fabrizio, C. Claudio, R.P. Alberto, A. Anastasia, A. Silvia Lucia, K. M. Youseuf, T. Francesco, *Materials (2021)*, 3, 1-20.
[2] K. Ilona, A. Silvia Lucia, T. Maria, H. Gjylije, C. Fabrizio, R.P. Alberto, C. Claudio, C. Roberta, T. Francesco, *Polymers (2020),* 5, 1–23.
[3] C. Fabrizio, T. Maria, C. Roberta, Z. Marco, T. Francesco, *Int. J. Pharm (2017),* 2, 470–479.
[4] B. Shahid, H. Maryam, I. Javed, R. A. H., M. M. A., A. N. A., W. S., R. K., R. S. *Polymers (2020),* 12, 1–60.

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KN02

Cyclodextrin-Based Polynitroxides For *In Vivo* Imaging

Lucio Melone[1,2]

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Cyclodextrins (CDs) can be used as building block for the synthesis of water-soluble supramolecular contrast agents (CAs) based on nitroxide radicals with MWs comprised between 5 and 6 kDa.[1,2] In presence of ascorbic acid (used to mimic the reducing environment of *in vivo* systems), CDs functionalized with nitroxides having a pyrrolidine structure showed a better stability than those with a piperidine structure. The relaxation enhancement was investigated under different magnetic field strength providing relaxivity values (r_1) comprised between 1.5 $mM^{-1}\,s^{-1}$ and 1.9 $mM^{-1}\,s^{-1}$ at 0.7 T while lower values were found at higher fields (r_1≈0.6-0.9 $mM^{-1}\,s^{-1}$ at 9.4 T). Tests *in vitro* on HEK293 human embryonic kidney cells, L929 mouse fibroblasts and U87 glioblastoma cells indicated that all compounds were non-cytotoxic at concentrations below 1 μmol mL^{-1}. MRI *in vivo* was carried out at 9.4 T on glioma-bearing rats. The experiments showed a good lowering of T_1 relaxation in tumor with a retention of the contrast for at least 60 mins confirming improved stability also *in vivo* conditions. [3] Some recent developments aimed at improving the relaxation properties will also be shown.[4]

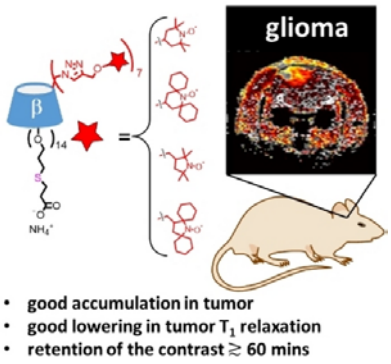

Figure 1. Some polynitroxides for MRI based on cyclodextrins.[3]

Acknowledgements: PNRR - RAISE - *Innovation Ecosystem Robotics and AI for Socio-economic Empowerment* – SPOKE 2, WP4 *Future of image-based diagnostic* is kindly acknowledged for partial funding.

[1] F. Caglieris, L. Melone, et al., *RSC Advances* (2015) *5*, 76133-76140.
[2] L. Melone, A. Back, G. Lamura, F. Canepa, R. Nivajärvi, V. Olsson, M. Kettunen, *ChemPlusChem* (2020) *85*(6), 1171-1178.
[3] L. Franco, A.A. Isse, A. Barbon, L. Altomare, V. Hypponen, J. Rosa, V. Olsson, M. Kettunen, L. Melone, *ChemPhysChem* (2023) 19(24), e202300100.
[4] L. Melone et al., *manuscript under preparation* (2025).

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KN03

Innovative One-Step SUPRADES Extraction: Enhancing Bioactive Compound Recovery

Miriana Kfoury[1], Johann Devillers[1], François-Xavier Legrand[2] and Sophie Fourmentin[1]

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[2]Université Paris-Saclay, CNRS, Institut Galien Paris-Saclay, 91400 Orsay, France

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Deep eutectic solvents (DESs) are the latest generation of sustainable and task-specific solvents made from solid components that form liquid eutectic mixtures through strong melting point depressions[1]. Recently, DESs based on binary mixtures of cyclodextrins (CDs) and other neutral components (*e.g.* levulinic acid, propanediol, lactic acid…) have been developed in the context of sustainable chemistry. These supramolecular deep eutectic solvents (SUPRADES), are attracting growing interest in many fields, like gases capture[2] or solubilization of bioactive compounds[3].
In this study, ready-to-use extracts suitable for cosmetic formulations were obtained in one step SUPRADES and microwave-assisted extraction (Figure 1). The extraction process was optimized in terms of SUPRADES components, temperature, water content and process time. Spent coffee grounds were used as a model food by-product due to their content of high value compounds.
The results showed that only 15 minutes were sufficient for simultaneous solvent preparation and extraction. SUPRADES were able to provide the highest extraction yields of antioxidants and polyphenols. In addition, the use of SUPRADES allowed obtaining stable and ready-to-use extracts with increased stability to oxidation, heat and light, as well as increased bioavailability.

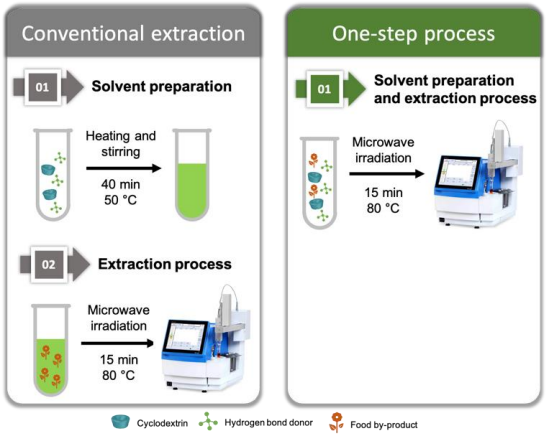

Figure 1. Representation of the conventional and one-step process.

Acknowledgements: This project is a part of the "Programme d'investissements d'avenir" (N° DOS0174861/00).

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[2] C. Gui, D. Xiang, M. Feng, C. Guo, S. Fourmentin, *Sep. Purif. Technol.* 360 (2025) 131121.
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KN04

Greener Rings: Sustainable Strategies for Cyclodextrin Derivatives

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Traditional syntheses of cyclodextrin (CD) derivatives often rely on harsh reagents and energy-intensive processes, raising environmental and efficiency concerns. Poor atom economy further compromises sustainability, while complex reactions and purification steps hinder scalability—highlighting the need for greener alternatives. Key derivatives such as 2-hydroxypropyl-β-CD (HPBCD), randomly methylated β-CD, and sulfobutylether-β-CD require highly reactive alkylating agents that are toxic, flammable, and volatile. CD intermediates like per-6-halogenated and per-6-silylated CDs are typically synthesized in organic solvents that are increasingly subject to regulatory restrictions. Cationic amphiphilic CDs—among the most promising CD-based excipients for nucleic acid delivery—require multi-step syntheses and chromatographic purification, which pose major barriers to industrial scalability. Likewise, water-soluble CD-based polymers derived from epichlorohydrin, citric acid, or nanosponge technologies rely on reactive crosslinkers and harsh conditions, leading to additional environmental and regulatory challenges. This work critically assesses production strategies for these CD derivatives, emphasizing recent advances in greener approaches aimed at process simplification, solvent and waste reduction, and enhanced industrial feasibility in line with green chemistry principles.

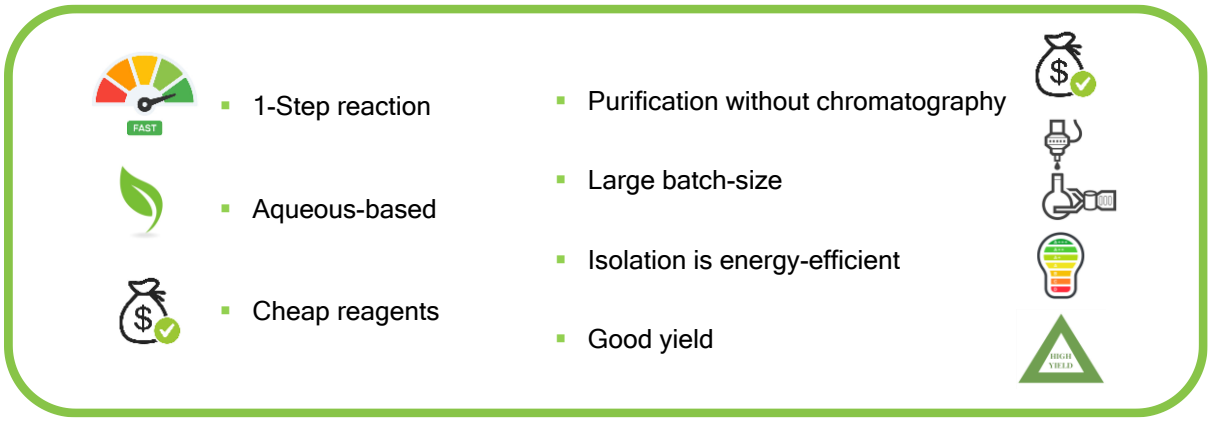

Figure 1. Overview of key parameters defining a green synthetic strategy.

Acknowledgements: HORIZON-MSCA-SE-01-01 2022 Bicyclos project #101130235.

Oral Presentations

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OP01

CD-polymers as supramolecular, hydrophilic platforms for phototriggered multicomponent reactions in flow

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To meet the target set by the EU Green Deal and significantly decrease human impact on the planet by 2050, a strategy is to prioritize safe and sustainable-by-design (SSbD) materials for the development of less impacting catalytic processes in homogeneous aqueous environment.

Cyclodextrin-polymers (CDPs) crosslinked with epichlorohydrin are able to i) organize in nanoparticles of diameter 20-50 nm, ii) increase the solubility of parent CDs up to 100 times and iii) co-solubilize more guests simultaneously, thanks to the assorted hydrophobic cavities and pockets.[1] Recently they have been shown to allow the photooxygenation of aromatic substrates at millimolar concentrations in water.[2] We further capitalized on the use of customized CDPs to perform highly efficient, photocatalytic reactions in homogeneous aqueous phase, in flow,[3] selected thiol-ene photo-additions and photooxygenations upon supramolecular loading of reactants into CDPs labelled with Photo-Active Ingredients (PAIs). Following a computational screening, the target reactions were optimized to achieve higher efficiency and selectivity in a photoreactor in flow.

With our first results we endorse our forecast on CDPs as blockbuster SSbD matrix to perform homogeneous photocatalysis in greener conditions enabling unprecedented large scale chemical productions and boosting novel pharmacological and environmental applications.

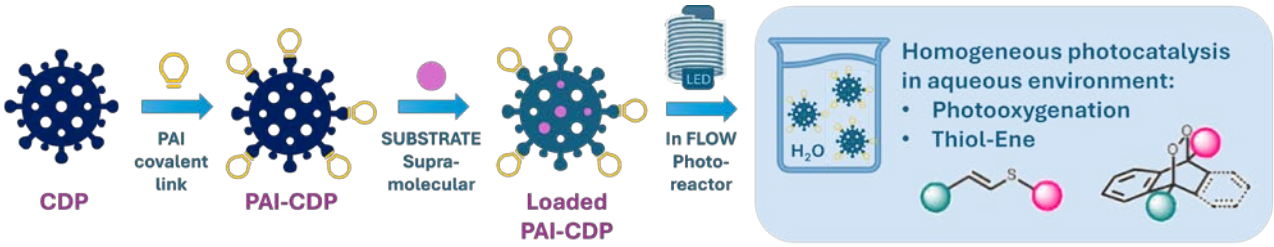

Figure 1. General strategy applying designed PAI-CDPs to the photo-induced conversion of organic substrates in homogeneous aqueous environment.

Acknowledgements: HORIZON-MSCA-SE-01-01 **2022** Bicyclos project #101130235; Fondazione di partecipazione ECOSISTER (ART-ER) Next Generation EU, PNRR-MUR.

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OP02

Immobilization of amphiphilic cyclodextrins on polypropylene by dip coating for PFAS removal

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Per- and polyfluoroalkyl substances (PFAS) are a group of manmade organofluoride compounds, which are bio accumulative, environmentally persistent and toxic to humans. Commercial adsorbents like activated carbon have limited adsorption of short chain PFAS and slow adsorption kinetics. A promising alternative adsorbent is cyclodextrin (CD) based materials. Most modification methods of surfaces with CDs require harsh organic solvents, long reaction times and/or advanced equipment [1]. We suggest an alternative method for immobilizing of amphiphilic cyclodextrins (ACDs) on polymeric materials which is simple, fast and only require household chemicals. The aim of this study is to modify polypropylene (PP) with ACDs and investigate how the degree of substitution (DS) and the ethanol/water ratio of the coating solution affect the removal capacity of PFAS.

ACDs with different DS were immobilized on non-woven PP by dip coating in a mixture of ACD, ethanol and water. Scanning electron microscopy (SEM) and contact angle measurements were performed to characterize the ACD coat, and the coat amount was determined using NMR with an internal standard. The removal of the PFAS was tested in static adsorption experiments.

SEM images illustrate that the ACD coat does not form a homogenous layer on the PP fibres but orientate itself into larger clusters (Figure 1). The static adsorption experiments showed that the DS has a significant effect on the removal capacity of PFAS of the ACD coated PP.

The results of this study demonstrate that non-woven PP easily can be modified with ACDs by a simple and quick dip coating to increase the removal capacity of PFAS.

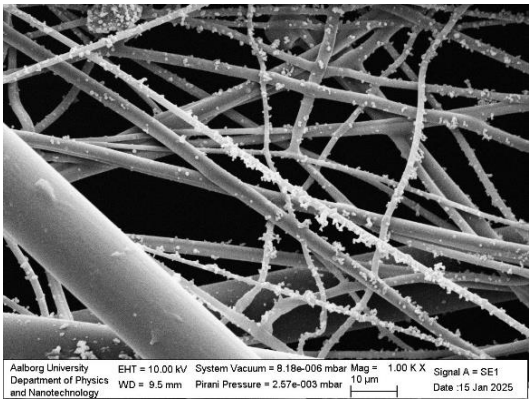

Figure 1. SEM image of ACD coated PP.

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OP03

Characterization of Cyclodextrin–Chlorhexidine interactions for the formulation of an eye drop against infectious Keratitis

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Infectious keratitis, a severe orphan disease, is caused by *Acanthamoeba sp*. and can lead to blindness or reduced visual acuity. The treatment of choice is the administration of a biguanide-based eye drop, such as chlorhexidine (CHx), which is prescribed off-label for this pathology. A significant challenge in formulating a CHx-based eye drop is a notably low degree of solubility in the presence of chloride ions, which are naturally present in tears. βCD/CHx complexes have been shown to enhance CHx's bactericidal activity while reducing its toxicity, suggesting a strong potential for their use in eye drop formulations [1].

The objective of this study is to evaluate the contribution of 5 cyclodextrins (CDs; αCD, βCD, γCD, HPβCD and RAMEB) in terms of stability and efficacy in a CHx digluconate eye drop formulation. The identification of CDs with the most effective stabilizing effect in the presence of chloride ions was undertaken, followed by the characterization of inclusion complexes using nuclear magnetic resonance (NMR) (Figure 1). The formation of inclusion complexes was confirmed by ROESY and DOSY NMR experiments, as well as ^{1}H NMR titration experiments. The latter experiments also allowed for the determination of binding constants [2], which varied depending on the use of pure CDs or CD mixtures.

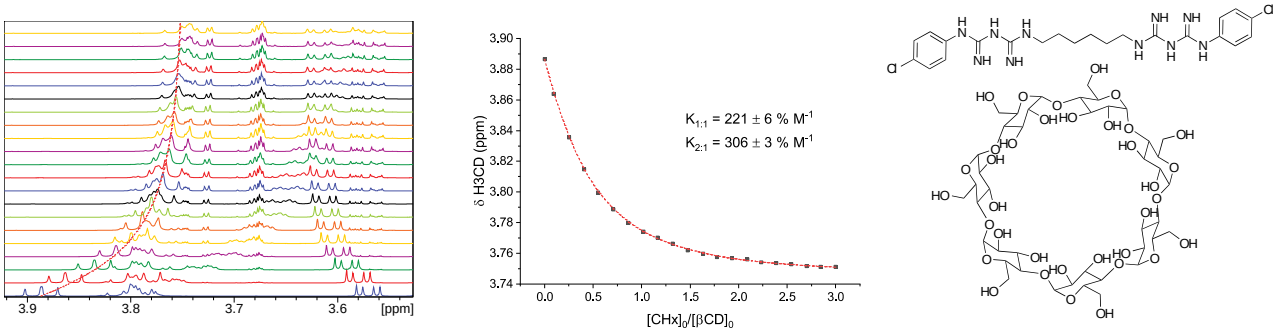

Figure 1. ^{1}H NMR (600 MHz, D_2O, 298 K) titration of βCD with CHx digluconate and the determination of the associated binding constant.

Acknowledgements: This work has benefited from the support of the "Université de Picardie Jules Verne" under "Booster Valo-CycloBig" project.

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OP04

Cyclodextrin-based supramolecular systems for polyphenols oral delivery: *in vitro* markers for *in vivo* permeation

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Natural polyphenols, such as rutin (RU), hesperidin (HES) and curcumin (CUR), possess multiple therapeutic activities, but their low solubility and low permeability in the GI tract hinder their use, making these substances interesting candidates for their complexation in supramolecular delivery systems for oral administration [1]. Therefore, β-cyclodextrins (CD), amphiphilic natural moieties able to form stable inclusion complexes, have been selected to promote the solubilization of RU, HES and CUR, and to demonstrate the possibility for the CD-drug complexes to be absorbed and to permeate *in vivo* by using an *in vitro* experimental setup, in view of a green approach [2]. The combination of different methods, including computational methods, diffusion and permeability studies have been considered as tools for predicting the *in vivo* performances. Hydroxypropyl-β-CD (HPBCD) and methyl-β-CD (MBCD), have been selected to investigate the effect of complexation of RU, HES and CUR. Phase-solubility studies, rationalized via docking calculations, revealed a strong complexation and an increased hydrophilicity of the systems. Drug diffusion profiles fitted on a computational technique, through a novel UV–Vis localized spectroscopy method, corroborated the high complexation constants, reducing the concentration of the free drug fraction available for permeation [3]. This result is reflected in the reduction of permeability through the PermeaPad® cell-free biomimetic barrier with respect to the drug in solution, demonstrating that the permeability is influenced by the type of CD. Then, in the case of CUR, specific indications of nano-supramolecular systems formation were recorded, supporting the precision of the fitting model. The computational approach shed light on the conformation of CD-based supramolecular systems as well on the strong binding responsible for the diffusion and the permeability of the drugs.

Acknowledgements: This work was supported by PON Ricerca e Innovazione 2014-2020.

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OP05

Nanohybrids based on amphiphilic β-cyclodextrin for magnetic delivery of a morphogen in microfluidic environments

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In tissue engineering, the spatio-temporal regulation of morphogens release is typically achieved using microfluidic devices [1]. Micro- and nanoparticles have been also experienced to deliver morphogens amounts directly onto stem cell cultures, but despite the efficacy of the method it can not offer precise control in the administration [2].
Here a supramolecular nanocarrier (SPION@SC6OH) composed of amphiphilic β-cyclodextrin (SC6OH) assemblies entangling superparamagnetic iron oxide nanoparticles (SPION) is presented and extensively characterized. We also demonstrate that the Retinoic acid (RA), a well-known differentiating agent for the neuronal cell line, loaded in the nanocarrier can be steered through microfluidic channels by external magnetic fields generated by a device based on actuated permanent magnets. This novel material can reliably deliver RA to in-vitro cell cultures and there induce differentiation of SH-5YSY cells into viable neurons having a minimum need of elaborated chip designs or advance pump/switch components. This technology enables the spatial- and temporal-controlled delivery of morphogens and could be integrated in microfluidic platforms for culture of patient-derived organoids in personalized medicine protocols [3].

Acknowledgements: This work was supported by the MUR-PNRR through the projects ECOSISTER (ECOSystem for sustainable transition of Emilia-Romagna) ECS 00000033 and SAMOTHRACE (SiciliAn MicrOnanoTecH Research And innovation Center) ECS 00000022, by MADMAN+ project - ISMN-CNR programme for scientific projects led by early-stage researchers - CNR Protocol Identification Number: 0001367.

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OP06

Complexation of cyclodextrin derivative with API's: an insilico approach

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Cyclodextrins (CDs) and their derivatives, notably methyl- and hydroxypropyl-substituted forms, are established solubilizing agents for active pharmaceutical ingredients (APIs) due to their capacity to form host-guest complexes. Solubility enhancement varies with the API and depends on the affinity between the CD derivative and the API. The mechanism driving this solubility increase remains sometimes elusive, as it hinges on the correct description of intermolecular interactions driving forces namely electrostatic interactions, van der Waals forces, hydrogen bonding, and charge-transfer interactions. Quantifying the affinity, thus the underlying forces in action, without resource-intensive experimental solubility studies is a pressing need in CD-based pharmaceutical research. A robust theoretical framework [1] has been developed to evaluate these complexation mechanisms and determine equilibrium, provided the stoichiometry (e.g., 1:1, 1:2) and key molecular interactions are accurately characterized. However, no widely accepted, transparent, or user-friendly in silico model currently exists to reliably quantify these interaction leading to the calculation of equilibrium/dissociation constants and finally phase solubility profiles for specific CD-API complex. This work introduces an in-silico workflow to assess complexation likelihood by integrating two complementary approaches. First, molecular dynamics simulations, paired with a generic force field, determine the most probable solution-state structures of the CD-API complex. Next, the statistically predominant conformations are analyzed using the COSMO-UCA method, developed by Roquette and the Pascal Institute [2,3], to compute activity coefficients, yielding complexation/dissociation constants used to determine the phase solubility diagrams. This approach offers a novel qualitative and quantitative approach for CD-API interactions, to help elucidate and try to quantify the molecular interaction at play in host-guest mechanism to advance rational design in cyclodextrin chemistry.

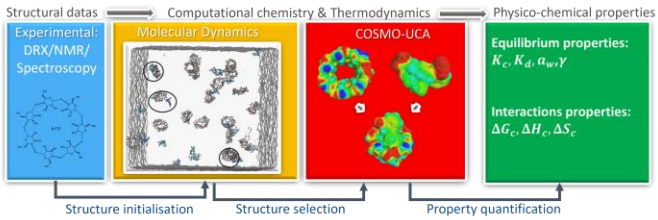

Figure 1 Insilico modelling workflow

This presentation showcases findings from a case study on valsartan in combination with Roquette Kleptose ® and Crysmeb® [4].

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OP07

Nanoparticles based on cyclodextrins polymers positively charged as drug delivery systems against glioblastoma

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The most common and malignant form of central nervous system (CNS) tumor in adults is glioblastoma multiforme and the widely used drug against it is Temozolomide. Unfortunately, it shows different side effects including neutropenia, thrombocytopenia, lymphopenia, and leukopenia. In this regard, research efforts have increasingly focused on developing systems that can enhance drug solubility, stability, and therapeutic efficacy [1].
In particular, nanosystems and nanoparticles have emerged as effective approaches for drug delivery [2]. Among these, cyclodextrins (CyDs), cyclic oligosaccharides composed of glucopyranose units, have gained significant attention due to their low toxicity and ability to form inclusion complexes with lipophilic drugs.
This work aims to investigate two polymers with positive charges for the delivery of two drugs. One is crosslinked at high molecular weight, and the other is linear at low molecular weight. This last system is synthetized started by a polymeric backbone of polyglutamic acid grafted with β-CyD preloaded with guanidinobutyric acid. The introduction of permanent positive charges in the polymers aims to facilitate crossing the blood-brain barrier [3–4].
Both the new linear polymer and the commercial cross-linked β-CyD polymer were investigated for the delivery of trametinib and selumetinib in glioblastoma cell lines. These two drugs, specifically designed to target MEK-dependent intracellular signaling pathways, suffer from poor solubility under physiological conditions and exhibit significant side effects. After the synthesis and characterization, the polymers were tested *in vitro* in two different glioblastoma cell lines (U251 and U87MG), showing that both drugs in the presence of carriers increase their activity, in particular the crosslinked polymer in the presence of selumetinib increase the antiproliferative activity more than 70%. The interaction of the polymers with the drugs will be investigated by NMR.

Acknowledgments: This work was partially supported by EU funding within the PRIN (Project no. 2022JXSA9C, SPlat-G).

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OP08

Cyclodextrin-AHL Hybrids: synthesis, characterization and effects on the LuxR-regulated bioluminescence

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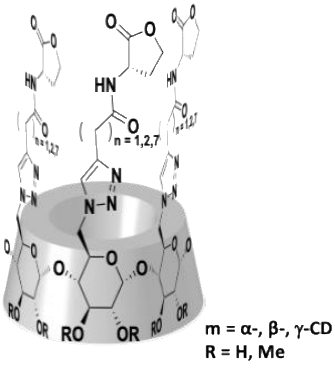
The phenomenon of Quorum Sensing (QS) has been identified in many Gram-negative bacteria and the most studied low-molecular-weight signal molecules are acyl homoserine lactones (AHLs), whose structural variations depend on the bacteria. Several AHL analogues have been shown to modulate QS *in vitro* with a wide range of potential applications [1]. Attaching biomolecules onto a cyclodextrin scaffold is a known strategy to enhance their properties [2], but designing CD-AHLs conjugates has never been reported. In this work, we have grafted AHLs onto cyclodextrins by CuAAC "click" coupling between alkynyl-AHLs and 6-azido cyclodextrins derived from α-, β- and γ-CD, native or methylated. These molecules were fully characterized by NMR and HRMS, and the study of their solubility and conformation revealed significant conformational changes due to the presence of the AHL appendage and the CD structure. One of the hybrids (perAHL-β-CD, **9_B**) exhibited higher solubility than AHL and β-CD alone. The new CD-AHLs conjugates were found to modulate bioluminescence in a QS LuxR-regulated light-producing bacterial model, with significant variations depending on the structure.



General structure of the final molecule

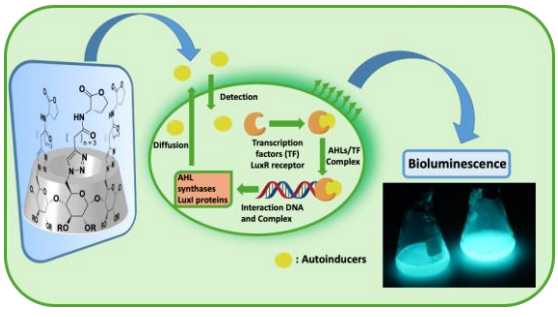
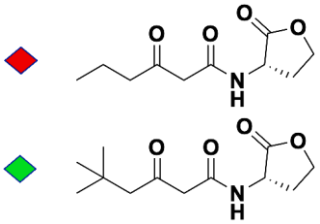


Diagram of the mechanism of action of QS



Examples of agonist (red) and antagonist (green)

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OP09

Continuous chiral separation of *rac*-voriconazole on liquid stationary phase containing cyclodextrins as chiral selectors

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In the context of enantioselective separations, the employment of chiral selectors is essential. The economic burden of cyclodextrins, a crucial component in enantioselective separation processes, poses a significant challenge in large-scale applications, necessitating the development of cost-effective methodologies. To this end, a novel method for the enantioselective separation of *rac*-voriconazole was developed, where chiral recognition occurs only when two immiscible liquid phases come into contact [1]. Centrifugal partition chromatography (CPC) is a liquid-liquid chromatographic technique where both the stationary and mobile phases are liquids, and the resolution is governed by the partitioning of solutes between these phases. In the course of our investigations, a variety of CD derivatives were examined as potential chiral selectors within diverse two-phase solvent systems, mostly utilized as stationary phases in the separation process.

Voriconazole, a widely applied antifungal medication, serves as a model drug for these investigations. Its synthetic process commonly yields a racemic mixture of (2*R*,3*S*)- and (2*S*,3*R*)-enantiomers, where the (2*R*,3*S*)-form is the eutomer, while the (2*S*,3*R*)-stereoisomer is the less potent distomer and its conventional purification method is chiral resolution [2].

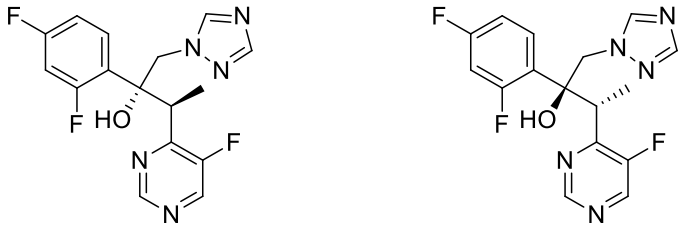

Figure 1: *Chemical structure of voriconazole enantiomers*

The study demonstrates that CPC technique for purifying racemic voriconazole *via* continuous multiple-dual mode (MDM) elution has resulted in a 15-fold increase in productivity compared to conventional resolution. This innovative approach has led to the production of 99.9% pure (2*R*,3*S*)-voriconazole, with excellent yield and high throughput, while conserving the valuable stationary phase containing the dissolved CD as a chiral selector, allowing its regeneration and recyclization.

Furthermore, the present study posits the hypothesis that a customized enantioseparation process is indeed feasible through the implementation of a centrifugal partition chromatographic approach.

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OP10

Light-Responsive Cyclodextrin-Based Platforms for Controlled Nitric Oxide Release

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Nitric oxide (NO) is one of the most studied molecules in the field of biomedical sciences, not only for its role as a signaling molecule in the human body but also as a promising unconventional therapeutic agent to tackle severe diseases, including cancer and bacterial infections. However, the strict dependence of its biological effects on concentration and site of generation requires precise spatiotemporal control over its delivery. Light activation of appropriate NO photoprecursors, namely NO photodonors (NOPDs), represents an optimal strategy, making the development of materials for triggering NO release within the therapeutic window highly desirable [1].

Cyclodextrin branched polymers (poly-CyDs) have recently emerged as valuable carriers in biomedical applications. These water-soluble, biocompatible polymers have proven to be excellent host systems for the complexation, stabilization and solubilization of a wide range of therapeutic and phototherapeutic guest compounds.

In this contribution, we present the design and development of novel light-responsive molecular systems and their supramolecular architectures using poly-CyDs. These systems allow precise, controlled NO photorelease triggered by blue light [2] with fluorescent reporting [3]. Furthermore, we introduce a supramolecular photosensitization strategy mediated by a red light absorbing photosensitizer coencapsulated with the NOPD in poly-CyDs, to shift the excitation wavelength toward a more biocompatibility and tissue penetrating light [4]. These innovative approaches offer promising advances for the treatment of cancer and bacterial infections.

Acknowledgements: We thank the European Union - NextGenerationEU through the Italian Ministry of University and Research under PNRR - M4C2-I1.3 Project PE_00000019 “HEAL ITALIA”.

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OP11

Evaluation of a Drug Delivery System based on Cycldextrins

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Many chemotherapy drugs are successfully used today, with, however, some limitations which include negative side effects and individual patient sensitivities. These limitations can be mitigated by drug delivery systems that can target cancer cells and deliver the therapeutic dose to the required site of action. In this study, cyclodextrins are used for targeting folate receptors (FR) and delivering the drug methotrexate (MTX). FRs are over-expressed in cancer cells and uptake of folic acid is mediated with high affinity by FRs. Uptake of antifolates, such as MTX, is mediated with high affinity by the reduced folate carriers (RFCs) and MTX acts by inhibiting folate metabolism.

This study addresses gene (mRNA) and protein expression levels of FRs and RFCs in a range of cell lines and cell viability assays were used to assess the cytotoxicity of folate-modified cyclodextrin CDEnFA and the complex CDEnFA:MTX. Results demonstrate that the complex showed greater cytotoxicity than the free drug towards the high FR expressing KB and CaCo-2 cells, indicating that it has potential to target this receptor, enhancing drug specificity and efficiency.

Protein inhibition was used to understand uptake of MTX and fumonisin-B1 and sulfasalazine were used to inhibit FRs and RFCs, respectively. The results demonstrated a decreased cytotoxicity caused by the MTX after inhibition of RFCs, confirming its internalisation through this transporter. The results also demonstrated that the cytotoxicity caused by CDEnFA:MTX is decreased after inhibition of each receptor and significantly decreased after a co-treatment that inhibits both transporters. This indicates that the cytotoxic effect from the complex CDEnFA:MTX can be a result of drug uptake through two routes shown in Figure 1: (1) The CDEnFA:MTX binds to FR on the cell membrane and this receptor internalises the whole complex by endocytosis. (2) after CDEnFA:MTX binds to FR, MTX is released from the cyclodextrin cavity and internalised through the RFC. By using both of these routes, CDEnFA:MTX can amplify the cytotoxic effect of the drug MTX.

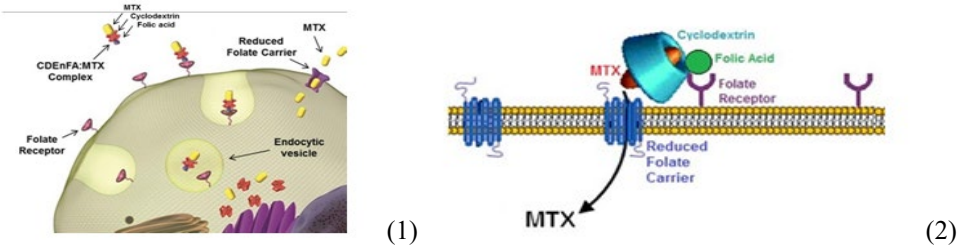

Figure 1: Folic acid targets the FR and (1) entire CDEnFA:MTX is internalised and MTX] is released in endocytic vesicles (adapted from Endocyte, inc) and (2), CDEnFA remains extracellular and MTX is internalised through RFC.

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OP12

Minireview on thermodynamics of aqueous surfactant-cyclodextrin complexes

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Detailed knowledge on surfactant-cyclodextrin interaction is crucial for precise modeling of (non)equilibrium processes in complex biologically, pharmaceutically, environmentally relevant and soft-matter aqueous matrices [1-5]. Thermodynamic quantities for (zwitter)ionic surfactant-cyclodextrin complexation compiled through ~30 literature sources are reviewed. The quantities are discussed in terms of their temperature dependence and structural features [6]. The observed thermodynamic footprint and stoichiometry of the formed complexes depend notably on alkyl chain length and type, head group polarity, cyclodextrin cavity size, and modification. Among the studied classes of surfactants and cyclodextrins, the alkylsulfates/α-CD and fluoroalkyl surfactants/β-CDs were identified as those with an exceptionally predominant interactions. The pitfalls to predict the cyclodextrin binding modes on double alkyl chain and catanionic surfactants from the binding of single chain surfactant bearing identical alkyl moiety, are addressed. Application of species distribution calculations on construction of ternary aqueous phase diagrams is shown for selected surfactant-cyclodextrin interaction.

Acknowledgements: Dedicated to the memory of prof. Miguel Antonio Costas Basín (1952-2024) from UNAM, Mexico. Financial support of this work from Institutional funding of the University of Chemistry and Technology Prague, is gratefully acknowledged.

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OP13

Cyclodextrin-drug conjugates – synthesis and study of their properties

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Drug delivery is the area where cyclodextrins (CDs) have found wide application due to their excellent solubility, low toxicity, and availability based on their low cost. Some types of anticancer drugs are problematic regarding stability, solubility, or adverse effects on healthy cells. Combined with CDs, these properties can be modified - using a covalent linker between the cyclodextrin and the drug molecule [1] also ensures better stability of the resulting conjugate across different conditions, such as pH and temperature changes.

By short biocompatible linkers, different CDs (α, β, and γ) were connected at position 6^I to a small anticancer molecule, 5-fluorouracil (FU) (Figure 1). These linkers were of varying lengths and expected to decompose under acidic conditions, allowing the drug to be released near tumor cells. All synthesized conjugates were based on 1-hydroxymethyl-5-fluorouracil connected to an appropriate linker by an ester bond – this connection enables the release of the unmodified drug, i.e., a different approach than previously published for CD-FUs [2]. Resulting conjugates were achieved by forming an amide bond between a linker and CD or a triazole ring from a click reaction between azido-CD and the terminal triple bond of a linker. Conjugates were fully characterized by conventional techniques (NMR, MS, and IR), and the stability and complexation properties of the synthesized conjugates were determined by 1D and 2D NMR experiments.

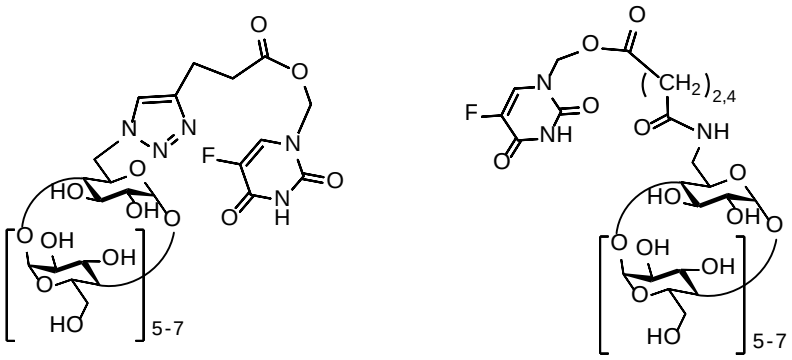

Figure 1. Prepared cyclodextrin-5-fluorouracil conjugates.

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OP14

Complexes from β-Cyclodextrin Derivatives for Water-Borne UV-Curable Semiconductive Nanocomposites with *in situ* AgNPs/PEDOT:PSS

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In photocurable polymeric materials the addition of nanomaterials, such as *in situ* formed silver nanoparticles and PEDOT:PSS, is capable of giving to the polymer matrix new mechanical and electro-optical properties.[1] Furthermore, the environmental impact of these nanocomposites could be improved by the usage of cyclodextrins, due to their capability of complexing oil-soluble components of a photocurable formulation in water, but also because of their low toxicity, high biodegradability, biocompatibility and availability.[2] In fact these advantages, together with the low VOC emissions, high efficiency and low energy consumption typical of the photocuring process, have the potential of making more sustainable polymer coatings for various industrial applications.[3]

Hence, this study aims to develop a water-based complexation system involving oil-soluble photoinitiators, diacrylates, and β-cyclodextrin derivatives. This system is subsequently used to prepare a UV-curable semiconductive nanocomposite coating which incorporates PEDOT:PSS and silver nanoparticles (AgNPs) generated *in situ* by photoreduction of a silver salt precursor (Figure 1).

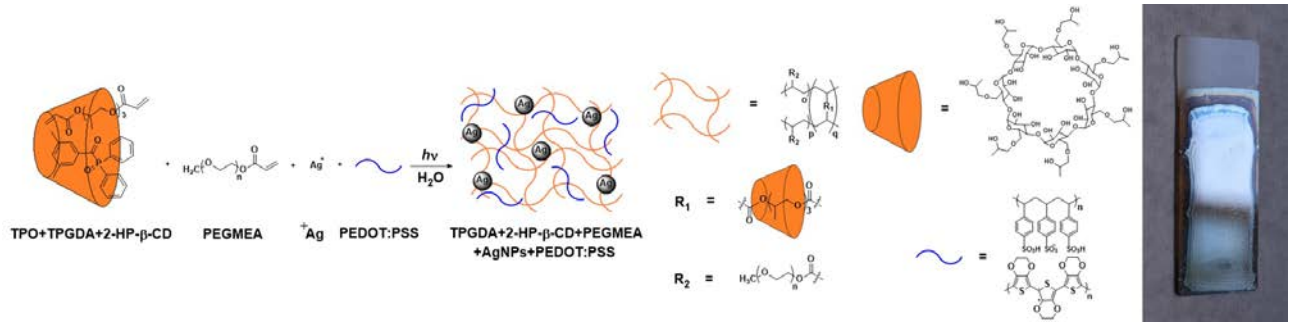

Figure 1. Production of an *in situ* AgNPs/PEDOT:PSS nanocomposite by photoirradiation of a β-cyclodextrin complex in water (left), and picture of the coated final material (right).

Acknowledgements: this project received funding from the #horizoneurope20212027 programme under the Marie Skłodowska-Curie Doctoral Networks (MSCA-DN) grant agreement No. 101073432.

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OP15

Cyclodextrins as Enabling Excipients for Nasal Dimethyl Fumarate Formulations

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Dimethyl fumarate (DMF) is marketed in oral capsules form, authorized by FDA and EMA, for the treatment of relapsing-remitting multiple sclerosis. Its use is often associated with severe gastrointestinal adverse events that may hinder its use in therapy. The drug is characterized by low aqueous solubility and low stability due to hydrolysis and sublimation at room temperature. To overcome these limitations, we evaluated the feasibility of using β-cyclodextrin derivatives, namely hydroxypropyl β-cyclodextrin (HPβCD), methylated β-cyclodextrin (RAMEB), and sulfobutylether sodium salt β-cyclodextrin (SBEβCD). Furthermore, since the nasal administration route has been studied for the delivery of active molecules directed to the central nervous system, due to the anatomical connection between the nasal cavity and the brain, the final objective of this study is to develop a formulation that can be administered nasally. This is also made possible by the presence of cyclodextrins as solubilizers and absorption enhancers [1], exploring an alternative administration route that optimizes the therapeutic efficacy of DMF.

The interaction between the drug and βCD derivatives was confirmed by physicochemical characterization using thermal analysis, FT-IR spectroscopy, and powder X-ray diffraction. Phase solubility studies highlighted how the concentration of the active substance increases linearly with increasing concentration of cyclodextrins.

A chitosan-based mucoadhesive nasally administrable powder was prepared using the DMF-RAMEB complex [2]. The use of RAMEB, associated to freeze drying method, appears to be a valid tool to overcome the problems related to stability and water solubility of the DMF.

HPβCD-DMF complex in a thermosensitive chitosan/glycerophosphate hydrogel could be able to promote the permeation of DMF released from the hydrogel across the nasal mucosa [3].

A thermosensitive poloxamer-based gel, containing chitosan as a mucoadhesive agent to deliver SBEβCD-DMF complex, was prepared and characterized for its physicochemical properties.

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OP16

Unraveling Niclosamide–HPβCD Interactions: From Complexes to Aggregates

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Niclosamide (Nic) is an FDA-approved oral anthelmintic drug with growing interest for repurposing in oncology, antibacterial, and antiviral therapies. However, its poor aqueous solubility (7.4 µg/mL) and low bioavailability limit its clinical applicability[1]. 2-hydroxypropyl-β-cyclodextrin (HPβCD) has been widely employed to improve the solubility of hydrophobic drugs through host–guest inclusion complexation, although evidence suggests that HPβCD-mediated solubilization may also involve non-inclusion interactions and aggregate formation[2]. In this work, we investigated the solubilization mechanism of Nic in the presence of HPβCD using a combined experimental and computational approach. ^{1}H NMR analyses confirmed that Nic forms 1:1 inclusion complexes with HPβCD; however, this interaction did not lead to increased solubility. On the contrary, a slight decrease was observed. However, higher HPβCD: Nic ratios (5:1 and 10:1) resulted in increased solubility values of 8.7 and 15.3 µg/mL, respectively. NMR data indicated that, under these conditions, Nic also interacts with protons on the outer surface of the macrocycle, suggesting the contribution of non-inclusion interactions. To gain molecular-level insights, we performed molecular dynamics simulations at various stoichiometries, incorporating both protonated and deprotonated forms of Nic. Simulations showed that Nic tends to form stable aggregates driven by π–π and cation–π interactions, limiting its solubility in water. In the presence of HPβCD, these self-associative interactions were disrupted. HPβCD molecules formed their own aggregates, with Nic arranging around them—either participating in host–guest inclusion or interacting at the hydrophilic surface—ultimately contributing to solubilization through a mixed mechanism.

Our findings highlight that HPβCD enhances Nic solubility not only through inclusion complexation, but also by interfering with Nic hydrophobic self-association via aggregate formation. This work emphasizes the importance of considering non-inclusion mechanisms in cyclodextrin-based solubilization strategies and offers valuable insights for the rational formulation of poorly soluble drugs like Nic for repurposed therapeutic applications.

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OP17

Mixed β-γ-Cyclodextrin Branched Polymer with Multiple Photo Chemotherapeutic Cargos

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Developing light-responsive materials for multimodal cancer therapies is a key challenge to enhance therapeutic outcomes through additive/synergistic actions while minimizing side effects.[1] In this study, it is presented a branched polymer based on β- and γ-cyclodextrins (βγCD-NOPD), integrating a nitric oxide (NO) photodonor (NOPD) within its macromolecular structure and supramolecularly encapsulating a singlet oxygen ($^1O_2$) photosensitizer, Zn(II) phthalocyanine (ZnPc), and the chemotherapeutic drug Lenvatinib (LVB).[2] The polymer, highly water-soluble, generates NO under blue light, with an efficiency more than 10-fold higher than NOPD alone. ZnPc, which is non-photoresponsive in water, becomes highly photoactive when encapsulated in βγCD-NOPD. Co-encapsulation of the poorly water-soluble LVB increases its solubility by over 30-fold. The supramolecular nanoensemble, about 15 nm in diameter, retains the photochemical properties of NOPD and ZnPc, enabling their parallel activation under blue and red light, respectively, to generate NO and $^1O_2$ accompanied by red fluorescence emission, and no LVB photodegradation. Notably, NOPD, ZnPc, and LVB do not show any undesired mutual interaction in both their ground and excited states, despite co-localization within the same host. The proposed polymeric nanoplatform offers a promising trimodal nanomedicine, merging the photodynamic effects of NO and $^1O_2$, two species not affected by multidrug resistance, with the therapeutic activity of a conventional chemodrug.

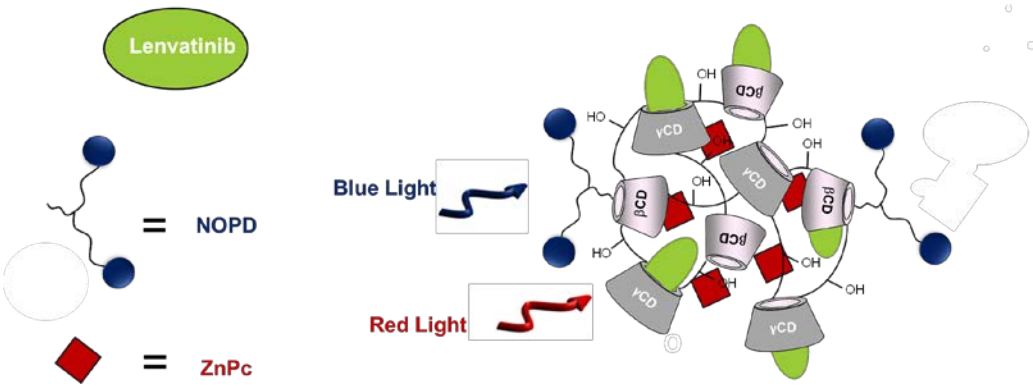

Figure 1. Schematic of the Trimodal Supramolecular Assembly

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OP18

Toxicological Profiling of Cyclodextrin-Based Deep Eutectic Solvents: *In-Vivo* Study on Organ Function and Gut Microbiota

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Deep Eutectic Solvents (DES) have emerged as promising alternatives to conventional organic solvents, providing enhanced solubility and stability for poorly water-soluble active substances. However, their toxicity profile remains insufficiently explored, particularly regarding their effects on organ function and gut microbiota. This study evaluates the *in-vivo* acute toxicity of various cyclodextrin-based DES formulations in Swiss mice following oral administration. The study involved key assessments, including biochemical markers for liver, kidney, and muscle function, histological analysis, and molecular profiling of the gut microbiome using 16S rRNA sequencing. The results demonstrated that cyclodextrin-based DES did not induce significant renal or hepatic toxicity, with stable urea levels, cystatin C, ALT, and AST. Muscle function markers (CK, LDH, and myoglobin) showed no indication of acute muscular toxicity. Additionally, gut barrier integrity was mostly maintained, although a slight downregulation of tight junction and mucus-producing genes was noted in the SBE-β-CD/Glycerol group. Microbial diversity analysis revealed no significant dysbiosis, with the overall taxonomic composition remaining stable post-treatment. Among the tested formulations, HP-β-CD/Propylene Glycol displayed the most favourable safety profile, making it a potential candidate for active substance solubility enhancement with minimal systemic toxicity. Future studies will focus on chronic toxicity evaluations and DES-active substance interactions to further establish their pharmaceutical viability.

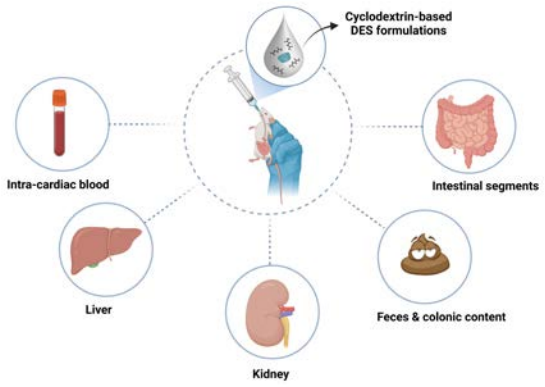

Figure 1. Overview of the safety study on cyclodextrin-based DES formulations.

Acknowledgements: We thank HEALTHI interdisciplinary program from Université Paris-Saclay for funding the MicroDES project and the ANR for supporting the ODES project (ANR-24-CE18-4929).

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OP19

Supramolecular materials based on cross-linked polyrotaxanes for optoelectronics

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The interest in slide-ring materials with slidable cross-linked macrocycle molecules has increased due to their ability to generate new smart functional materials [1]. The pulley-like property of the mobile junctions acquires both stress dissipation and actuation of the resulting materials. Herein, we proposed the synthesis of the composite materials based on polyethylene glycol (PEG) and polypyrrole (PPy) polyrotaxanes both encapsulated into α-cyclodextrins (α-CDs) macrocycle molecules. It was observed that the PPy-αCD cross-linked into the matrix has a beneficial effect on thermal and dielectric properties compared with the reference material. More than that, conductivity measurements at 10 Hz frequency indicated three orders of magnitude higher for the material with PPy-αCD polyrotaxane than the reference material. Raman spectroscopy provided additional information, which was possible to correlate the structural characterization with the conducting properties of these materials [2].

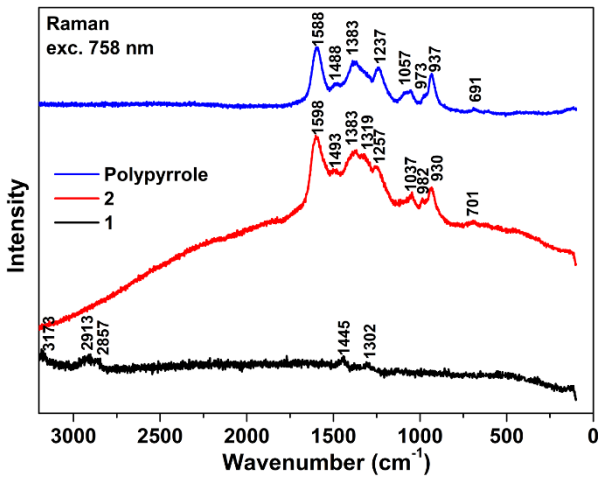

Figure 1. Raman spectra of composite materials with PPy-αCD (**1**), reference material **2** and polypyrrole polymer.

Acknowledgements: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS-UEFISCDI, project number PN-IV-P1-PCE-2023-0300, within PNCDI IV.

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OP20

CRYSMEB® : a « new » tool in the excipient market

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Methylation of cyclodextrin is a well-known chemical modification to have access to a new range of ingredients for various purposes (pharmaceutical application, analysis, cosmetics…). Many methylated derivatives are already available in the market (TRIMEB®, RAMEB®, DIMEB®, CAVASOL W7 M® …) and many prototypes have already been generated by modification of the reaction conditions, to afford molecules with different molecular substitution level, different patterns of substitution.

Though described in the literature for many years, characterisation of these products remains a challenge to link their composition to their properties [1].

Among these methyl-B-Cyclodextrin derivatives described approximately 30 years ago by J. Pitha [2] is CRYSMEB®. CRYSMEB® has been used in many comparison studies and exemplified in many articles and has shown a great potential in complement of other already available molecules. But what is CRYSMEB®? What is the specificity of this cyclodextrin derivative? What about its toxicity, especially the impact of molar substitution in regard with other available methyl cyclodextrins [3,4, 5]? With this presentation we would like to come back on its characterisation, it's specificity and some interesting properties that have been demonstrated and that might make CRYSMEB® a new tool for future pharmaceutical developments.

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OP21

Cyclodextrin-aided repurposing of disulfiram-loaded electrospun nanofibers for glioblastoma therapy

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Disulfiram (DSF), an FDA-approved drug used for chronic alcohol dependence, has shown potential as a versatile anticancer agent in the treatment of various cancers, including glioblastoma (GB) [1]. Its mechanism of action involves the chelation of Cu(II) in cancer cells, forming a copper-DSF complex ($Cu(DDC)_2$), which induces reactive oxygen species toxicity and promotes apoptosis. DSF also acts as a proteasome inhibitor, targeting protein turnover pathways, inducing endoplasmic reticulum stress, and inhibiting efflux pumps. In addition to its anticancer properties, DSF exhibits anti-inflammatory and antibacterial activities, which may be beneficial in preventing infections after tumor resections in GB patients. However, DSF's clinical application is limited by its low solubility, short plasma half-life, and toxicity at high doses, highlighting the need for local delivery devices.

This study focuses on developing an electrospun scaffold for localized treatment of recurrent GB, utilizing silk fibroin (SF) as the structural polymer, hydroxypropyl-β-cyclodextrin (HPβCD) for drug encapsulation [2], and $CuCl_2$ as a copper source. The electrospun mats allowed for in situ formation of $Cu(DDC)_2$, boosting both antimicrobial and antitumoral effects. In vitro studies demonstrated selective toxicity against glioblastoma cells while sparing normal astrocytes, indicating the targeted nature of the nanofiber system. The combination of DSF, SF, HPβCD, and Cu(II) resulted in enhanced therapeutic potency at low drug concentrations. In vivo studies in a rat model confirmed the safety of DSF-loaded electrospun fibers in healthy brain tissue post-surgery. While the DSF-loaded fibers alone did not completely eradicate tumors, the results suggest their potential as part of a combination therapy regimen. The optimized formulation provides a promising approach to overcome the limitations of current GB treatments, offering a more precise and effective method for drug delivery and tumor targeting [2].

Acknowledgements: The work was supported by Spain Ministerio de Ciencia, Innovación y Universidades MICIU/AEI/ 10.13039/501100011033 [PID2023-150422OB-I00], ERDF A way of making Europe, cofunded by the European Union, and Xunta de Galicia [ED431C 2024/09].

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OP22

Comparative Study of β- and γ-Cyclodextrins Functionalizations for Polysaccharide System Grafting

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Cyclodextrins (CDs) are frequently functionalized with a variety of chemical groups to improve aspects such as solubility in water, especially beta-cyclodextrin (β-CD), ability to include other molecules in their hydrophobic cavities and reducing toxicity when ingested [1]. Due to the presence of the hydroxyl groups, CDs easily lend themselves to chemical modifications, which can also be performed to create more complex systems, such as polymer conjugates, thus further expanding their fields of application in many areas [2]. In this study, the functionalization of β-CD and gamma-cyclodextrin (γ-CD) using maleic and succinic anhydrides was studied and the chemico-physical properties of the products were compared. The degree of functionalization, determined by 1H NMR spectroscopy, was 25% and 11% for β-CD and γ-CD derivatives of maleic anhydride respectively, and 40% and 25% for β-CD for γ-CD respectively when succinic anhydride was used. The thermal properties of the functionalised CDs also confirmed the introduction of carboxylic groups which increased the solubility in water of the new products with respect to the native CDs. Moreover, the presence of these new groups facilitated their conjugation with chitosan (CS), a polysaccharide with extremely versatile properties [3]. The formation of CS-CD matrices made from both CDs was confirmed by 1H NMR and FT-IR spectroscopic techniques, their thermal characteristics were determined by using DSC/TGA, while the morphology of their 3-dimentional structures, obtained by freeze-drying, was investigated using FE-SEM. The swelling properties of all matrices confirmed the effect of CDs on the properties of CS. Finally, the ability of the systems to encapsulate curcumin (CUR), a highly hydrophobic molecule, was evaluated by comparing the performance of the chitosan-only matrix with that of the grafted polymer (Figure 1).

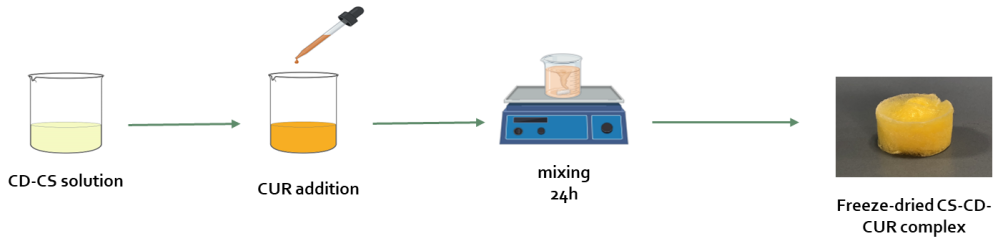

Figure 1. Scheme about the preparation of chitosan-cyclodextrins polymeric matrices containing curcumin.

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OP23

Enhancement of natural cyclodextrin's structural rigidity via primary alcohol-to-nitrile or amide transformation. Evaluation of the complexation properties.

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Cyclodextrins (CDs) are cyclic oligosaccharides widely used for their ability to form inclusion complexes, thereby modulating the solubility and stability of guest molecules. The present research focuses on the selective functionalization of CDs by converting primary alcohol groups into nitriles and further to amides. These reactions were conducted on α, β and γ CDs. The key step involves the chlorination of CDs primary amines [1] which results in the formation of highly chlorinated molecules containing up to 16 chlorine atoms (Figure 1). The structures of these intermediates, as well as the target nitrile and primary amide derivatives, have been confirmed by extended high-resolution mass spectrometry (HRMS) and NMR experiments. Theses transformations increase the rigidity of primary faces by reducing hydroxyl rotation and reinforcing hydrogen bonding interactions, leading to a structural expansion of CDs cavities. The encapsulation efficiency of these new molecular cage compounds was evaluated for resveratrol and compared with complexes previously reported using β-CD and RAMEB.[2] This study opens new perspectives in the field of host-guest supramolecular chemistry and provides a rational approach to design advanced cyclodextrin-based materials with tailored inclusion properties.

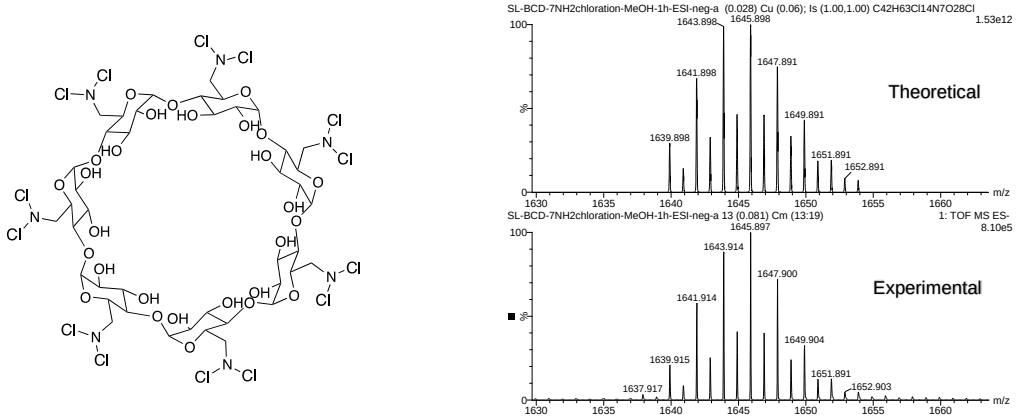

Figure 1. Structure of chlorinated amino β-CD ($C_{42}H_{63}Cl_{14}N_7O_{28}$) and comparison of the experimental isotopic pattern of its $[M+Cl]^-$ obtained in ESI^- with the theoretical one.

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OP24

DEWY: Biodegradable Nanosponge-Based Hydrogel for Sustainable Water Management in Viticulture

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Climate change is significantly affecting agriculture, particularly viticulture, where water scarcity threatens both yield and quality. Conventional solutions, such as petroleum-based hydrogels, present environmental concerns due to the release of microplastics into the soil.

Dewy offers an innovative, biodegradable hydrogel made mainly from starch derivatives including cyclodextrins, designed to enhance soil moisture retention while gradually releasing nutrients. Capable of absorbing up to seven times its weight in water, it ensures sustained hydration for vines, reducing irrigation demands and promoting plant health.

Unlike traditional hydrogels, Dewy naturally decomposes, enriching the soil with prebiotic organic matter that foster microbial biodiversity. This sustainable alternative aligns with the European Union's regulations on microplastics in agriculture, providing an eco-friendly solution.

Currently validated in laboratory conditions, Dewy is undergoing controlled greenhouse trials to assess its effectiveness before expanding to field applications. Our objective is to deliver a cost-effective, scalable solution for vineyards in drought-prone regions, ensuring both economic sustainability and environmental responsibility. This research-driven innovation marks a significant step toward sustainable water management in viticulture, with potential applications across broader agricultural sectors.

Acknowledgements: A.M. Thanks for its Ramón y Cajal Contract funded by MICIU/AEI/10.13039/501100011033 and by the FSE+ (Grant RYC2023-043196-I). DEWY is part of a Proof of Concept project funded by CDP Venture Capital (Italy).

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OP25

A little cyclodextrin here, a little cyclodextrin there

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Cyclodextrins (CDs) are everywhere. This presentation offers a review-based analysis of currently marketed CD-containing drug products, with a specific emphasis on APIs that are commercialized in more than one dosage form or administered *via* different routes. A key focus is placed on identifying and comparing those APIs that exist in multiple CD-based formulations, sometimes different types of CDs are employed depending on the formulation needs.

By reviewing data from scientific publications, review articles, and patent documents, we aim to uncover formulation strategies that use the versatility of CDs across various pharmaceutical platforms. The presentation discusses the choice of CD types in each dosage form, as well as how their physicochemical and regulatory properties influence product development. Trends in dosage forms, routes of administration, therapeutic indications, and the role of CDs in overcoming formulation challenges are also explored in detail.

The review highlights both well-established CD-based products and identifies potential gaps in the market, cases where promising CD-API combinations have been proposed in the literature or patents but are not yet commercially available. This analysis aims to inform and inspire formulation scientists and developers by showing the formulation flexibility of CDs and pointing toward new opportunities for innovation in drug delivery.

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OP26

A supramolecular assembly made with sulfobutylether-β-cyclodextrin and magnetic Fe_3O_4 showing water remediation properties

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In literature many examples of magnetic nanohybrids based on cyclodextrins are reported, but they often require multistep processes and preliminary synthetic efforts that affect the scale-up for the final application. In this work, a magnetic hybrid system was produced by supramolecular self-assembly between low-cost precursors: the sulfobutylether-β-cyclodextrin (Captisol®) and magnetic iron oxide-based nanoparticles (MNPs). The interaction between the two was elucidated by spectroscopic (FT-IR, XPS, μXRF) and imaging (TEM) techniques. The resulting MNPs@Captisol assembly was characterized by TGA and the magnetization properties compared. The colloidal features were evaluated by DLS measurements and an adapted turbidimetric analysis. Finally, a promising use of MNPs@Captisol as remediation agent against paraquat (chosen as a model of cationic pollutant), has been demonstrated. The sequestering mechanism was ascertained to be driven by electrostatic complexation.

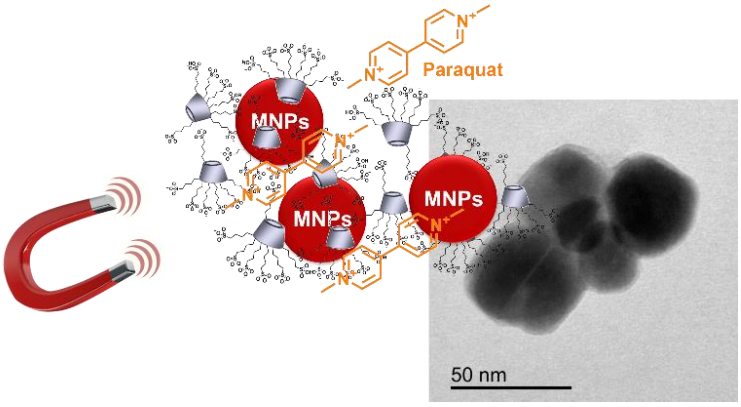

Figure 1. Graphical abstract

Acknowledgements: This work was supported by the MUR-PNRR through the NextGenerationEU program with the project SAMOTHRACE "SiciliAn MicrOnanoTecH Research And innovation CEnter"; the MUR-PON "Ricerca e Innovazione" 2014-2020, Azione IV.5 "Dottorati e contratti di ricerca su tematiche Innovazione and green"; and the University of Catania from the PIA.CE.RI. project. Authors thank the B.R.I.T. laboratory of the University of Catania for the availability of the XPS facility and Ligand (San Diego, CA-USA) for Captisol®.

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OP27

Preparation, characterization and activity of anticancer drugs encapsulated in β-cyclodextrin nanosponges

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Cyclodextrin (CD)-based polymers and nanoparticles offer significant opportunities in drug delivery due to their high drug loading capacity, low cytotoxicity, and the ease of surface functionalization, which enables targeting of specific cells. In our laboratory, β-cyclodextrin (β-CD)-based nanosponges (CNs) were synthesized using two different crosslinkers—citric acid and epichlorohydrin—by varying the β-CD/crosslinker ratios. The resulting CNs exhibited particle sizes ranging from 100 to 50 nm and carried a negative surface charge between −30 mV and −15 mV. After purification, the epichlorohydrin-crosslinked CNs were further modified with 3-aminopropyltriethoxysilane (APTES) to generate positively charged CNs.

These CNs, which possess both hydrophobic and hydrophilic domains, were used to co-encapsulate two anticancer drugs: N, N-bis (5-ethyl-2-hydroxybenzyl) methylamine (EMD) and doxorubicin, that act through different mechanisms on cancer cells. EMD promotes apoptosis through c-Myc suppression while doxorubicin damages DNA and stops cancer cells growth. Successful drug encapsulation was confirmed using NOESY NMR spectroscopy, and in vitro drug release studies were conducted. Cellular uptake and cytotoxicity studies of drug-loaded CNs were performed on human lung cancer cells (A549), human breast cancer cells (MCF-7), and normal human lung fibroblast cells (WI-38).

Results demonstrated synergistic cytotoxic effects against cancer cells when both drugs were co-encapsulated, enabling the use of lower drug doses compared to single-drug treatments, with potential decrease on drug side effects. Furthermore, the CNs loaded with two drugs exhibited higher cytotoxicity toward cancer cells than toward normal cells. These findings suggest that β-CD-based nanosponges are promising nanocarriers for the co-delivery of anticancer agents, enhancing therapeutic outcomes through improved efficacy and cell specificity.

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OP28

Exploring Enzymatic Degradation, Reinforcement, Recycling and Upcycling of Poly(ester)s-Poly(urethane) with Cyclodextrin as Crosslinks

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Polymeric materials, which are mainly composed of petroleum, are required to achieve a low environmental impact. To address polymeric waste in an eco-friendly method, researchers have focused on enzymes as highly efficient, chemoselective and renewable biocatalysts [1]. We have successfully proposed several designs to control the stability and enzymatic degradation of polymeric materials by introducing reversible and movable cross-links [2,3].

Reinforcement of poly(ε-caprolactone)-polyurethane (P(ε-CL)-PU) with movable cross-links [3]: We have prepared movable cross-linked poly(ε-caprolactone)-polyurethane (P(ε-CL)-PU) with triacetylated γ-cyclodextrin (TAcγCD) (Figure 1a). The obtained materials show high toughness due to stress dispersion.

Repolymerization and degradation of P(ε-CL)-PU with movable cross-links [3]: The degradation efficiency catalyzed by lipase was optimized for increases in TAcγCD content, due to the bulkiness of TAcγCD introducing more free volume in polymer network. Closed-loop recycling was achieved by switching the reaction concentration and temperature using the same enzyme, or enzymatically upcycling into value-added polymers by mixing with selective substrates.

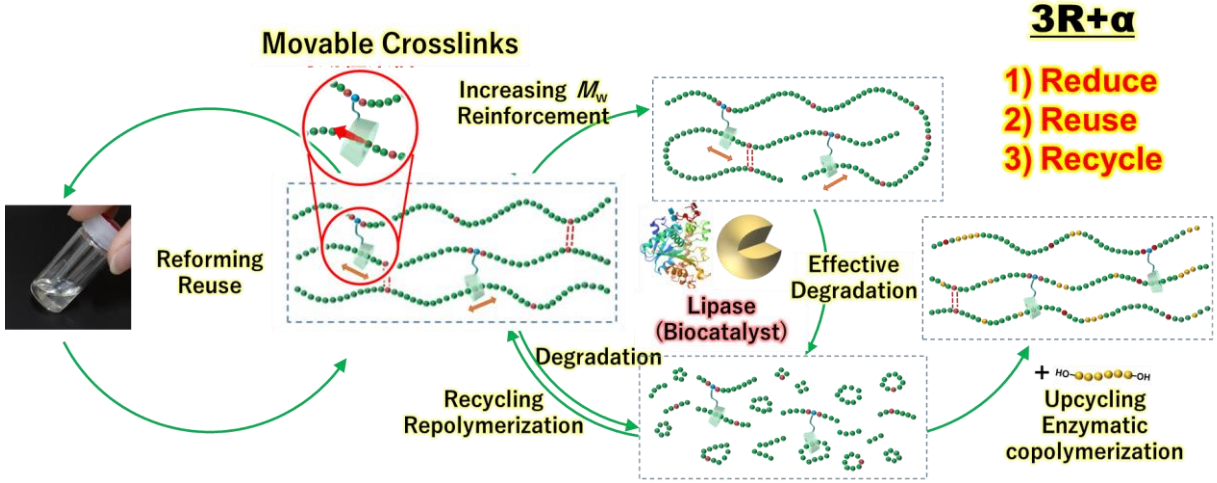

Figure 1. Controlling of mechanical properties and enzyme-catalyzed reaction with movable cross as cyclodextrins.

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OP29

Supramolecular hybrid nanomaterials composed of metal nanoparticles and cyclodextrins for health applications

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Cyclodextrins (CDs) are widely exploited as components of supramolecular functional hybrid nanomaterials in virtue of their well known ability to complex a variety of chemical species within their cavity through host- guest interactions. In combination with inorganic nanomaterials, CDs provide biocompatibility and stability which are very important for biomedical applications [1, 2]. Hybrid nanoassemblies composed of CDs covering metallic nanoparticles (NPs) are here shown. Gold NPs decorated with monomeric or polymeric CDs have been synthesized, showing complexing properties towards drugs as dopamine [3] and 5- fluorouracil. Interestingly, polymeric CD acts also as reducing and stabilizing agent towards Ag and Au precursors, allowing to obtain stable metal NPs. In particular, Ag NPs show promising antibacterial properties against *S. aureus.* In order to achieve a photo-antibacterial effect, the interaction with organic chromophores as porphyrins has been also studied. The nanoassemblies have been characterized through a combination of spectroscopic techniques as UV/Vis absorption, steady- state and time-resolved fluorescence, DLS and ζ-potential measurements.

The high versatility of CDs and of our synthetic approach based on supramolecular interactions allow to prepare functional nanomaterials for several applications, as drug delivery systems and for environmental sensing.

Acknowledgements: This work has been funded by European Union- NextGenerationEU, through PRIN 2022 PNRR project (HO-Hybrid[2], Prot. P2022F4PTE, CUP B53D23025690001) and partially by MUR-PNRR through SAMOTHRACE project (SiciliAn MicrOnanoTecH Research And innovation Center, ECS 00000022).

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OP30

Cyclodextrin-assisted bio-click chemistry applied for obtaining maritime pine bark extract-based and silymarin-based lipopolyphenols by enzymatic synthesis

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Bio-click chemistry is a recent technique combining classical click chemistry (parallel, orthogonal and simple reactions for obtaining groups of derivatives with high selectivity and yields, but low by-product levels) and the stereoselective biocatalysis or enzymatic synthesis [1]. Natural polyphenols having antioxidant activity are less stable and highly hydrophilic, being difficult to cross hydrophobic barriers/membranes. It is the case of the best hepatoprotective silibinins from silymarin (*Silybum marianum* extract, "Sm") or procyanidins and chlorogenic acids from the maritime pine (*Pinus pinaster*) bark extract/Pycnogenol® ("Py") [2]. Sm and Py extracts were derivatized to their fatty acid (FA) esters/lipopolyphenols using the bio-click chemistry technique. Enzymatic synthesis was performed in the presence of natural cyclodextrins (CDs), using Novozym 435®, Sm or Py:FA:CD molar ratio of ~1:1:1, temperature 40 °C, time 120 h and DMSO as solvent (Figure 1). The performance of the bio-click chemistry derivatization and CD complexation were evaluated by RP-HPLC, thermal and spectroscopic techniques. CD-assisted bio-click chemistry proved to be a valuable "eco-friendly" technique for "one-pot" bioconjugation and CD complexation for obtaining new lipopolyphenols and their CD complexes with high expected bioavailability and bioaccesibility.

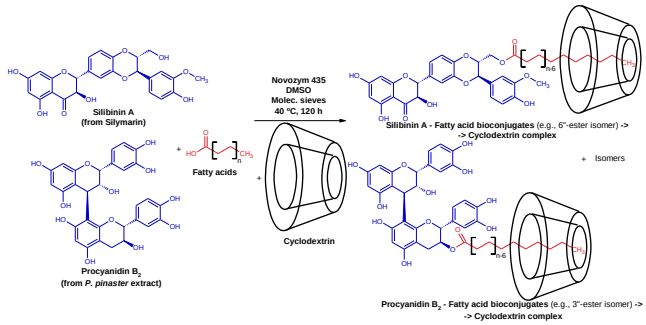

Figure 1. Schematic representation of the cyclodextrin-assisted bio-click chemistry technique applied to silymarin (*S. marianum*) and *P. pinaster* extract derivatization and complexation.

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OP31

Harnessing HP-β-CD in zein edible coatings for enhanced food preservation

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Increasing environmental, ecological, and safety concerns over the use of petrochemical-based, non-biodegradable packaging materials have intensified the search for sustainable alternatives [1]. Biodegradable and compostable materials derived from renewable sources, such as lipids, polysaccharides, and proteins, are gaining prominence. Among them, prolamins, the main storage proteins of cereals, offer unique potential [2]. Zein, a corn-derived prolamin, has emerged as a promising candidate for food packaging due to its excellent film-forming ability and its high content of hydrophobic amino acids, which impart favorable water and gas barrier properties. However, the brittle nature of zein films limits their standalone application [3].

To overcome this limitation, we incorporated 2-hydroxypropyl-beta-cyclodextrin (HP-β-CD) as a functional additive, capitalizing on its ability to interact with hydrophobic amino acid residues in zein. We systematically investigated the effect of HP-β-CD on zein aggregation under different conditions of temperature, ethanol concentration, and protein content. Using dynamic light scattering (DLS), transmittance and fluorescence emission analyses, we observed that HP-β-CD effectively reduced zein aggregation, enhancing solubility. Optimized zein dispersions (90% v/v ethanol) were subsequently used to prepare flexible films by adding polyethylene glycol (PEG 400) as a plasticizer. Structural and physicochemical characterization revealed that the inclusion of HP-β-CD significantly improved surface uniformity and barrier properties, notably reducing water permeability and light transmission. These enhancements are attributed to the formation of a denser, more cohesive polymer matrix which was further supported by Scanning Electron Microscopy (SEM) images.

Finally, zein/HP-β-CD dispersions were applied as edible coatings on strawberries via dipping. The resulting coatings extended fruit shelf life without requiring additional active ingredients, underscoring the system potential for natural food preservation. This scalable and clean-label approach offers a compelling pathway toward sustainable, functional packaging solutions and merits further investigation across a broader spectrum of perishable food products.

Acknowledgements: This work is dedicated to the memory of Professor Alberto Ritieni, Founder and Director of the PhD Course in Nutraceuticals, Functional Foods And Human Health at the University of Napoli Federico II, who prematurely passed away.

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OP32

Understanding the Kinetics of Eugenol adsorption and release through β-CD based microcapsules and Metal Organic Frameworks

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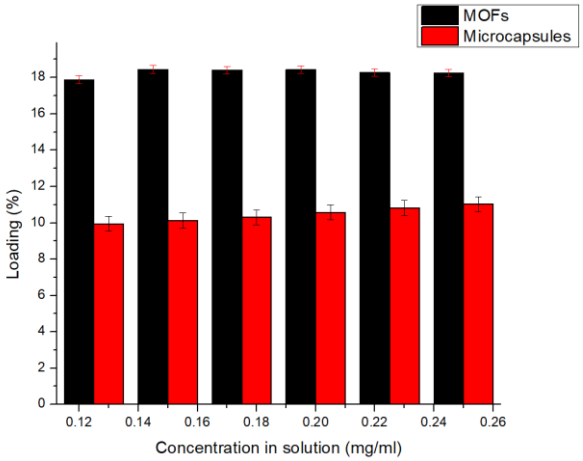
The application of volatile compounds like essential oils in fields such as pharmaceuticals and packaging is frequently limited due to their low stability under environmental conditions. We have tried to overcome the issue by developing β-CD based microcapsules and metal organic frameworks. The microcapsules were prepared by following the steps as mentioned by Kong et.al.[1] and the MOFs were prepared by vapour diffusion technique. Eugenol was used as active principle. XRD analysis showed MOF structure with 76% crystallinity and porous layered structures consisting channels was observed through SEM. The FT-IR results indicated that no eugenol was present on the surface and was completely incorporated inside MOFs cavities. The loading efficiency of MOFs were around 18±0.5% irrespective of amount of MOFs while the microcapsules showed loading ranging from 9-11% depending on the amount of microcapsules. This referred to homogenous distribution of eugenol in MOFs. The absorbance of eugenol inside the MOFs was monitored over time and pseudo second order model was found to be best fit with R^2 = 0.96492 as compared to that of R^2 = 0.93716 in pseudo first order and R^2 = 0.91244 in Weber-Morris Model.



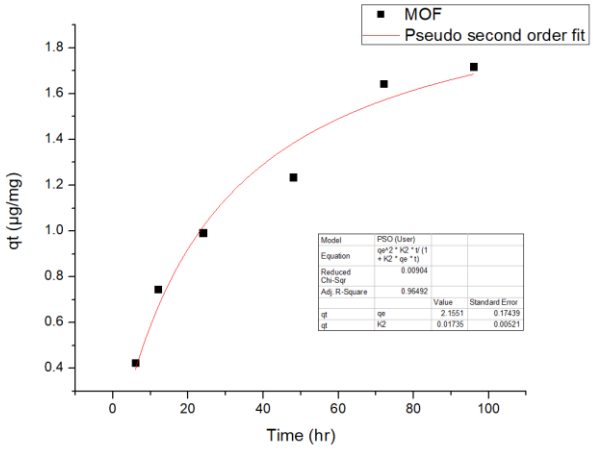


Figure 1. Loading percentage of Eugenol in MOFs and microcapsules and Figure 2: Adsorption kinetics of Eugenol on MOFs following Pseudo second order

Acknowledgements: The authors would like to thank GENCAT-AGAUR (Agència de Gestió d'Ajuts Universitaris i de Recerca)

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OP33

Advanced Cyclodextrin-Functionalized Systems for Water Purification

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Micropollutants are contaminants that occur in the aquatic environment at extremely low concentrations, yet they can have significant adverse effects on human health, wildlife, and entire ecosystems. These include residues of pharmaceuticals, pesticides, hormones, heavy metals, and industrial chemicals. As the European Union introduces stricter regulations, there is a growing demand for advanced tertiary wastewater treatment technologies capable of effectively removing these persistent pollutants.

In this contribution, we present a cyclodextrin-based approach to the removal of micropollutants from water [1], focusing on β-cyclodextrin polymers immobilized onto electrospun nanofibers. The resulting nanofiber composite exhibits high affinity for hydrophobic pharmaceutical pollutants such as pimavanserin, an antipsychotic drug known for its persistence and toxicity in the aquatic environment. The cyclodextrin-functionalized nanofibers combine the high surface area and structural stability with the molecular recognition capabilities of β-cyclodextrin.[2]

Batch adsorption studies revealed that the nanofiber-supported polymer exhibited superior kinetic performance and higher equilibrium adsorption capacity compared to the free polymer in suspension. Moreover, the system maintained high efficiency across a broad pH range, making it suitable for practical wastewater treatment scenarios. These findings underscore the potential of cyclodextrin-functionalized nanomaterials as scalable and environmentally friendly adsorbents for advanced water purification technologies.

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OP34

Cyclodextrins and entropy: lighting up grey zones

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The development and optimization of cyclodextrin-based applications require accurate knowledge of structure. Single-crystal XRD studies provide necessary information about cyclodextrins structure. However, single crystals cannot be obtained many CD application cases: crystalline and amorphous powders, solutions, gels etc. Such formulations constitute the majority of industrial CD applications. The universal thermodynamic relationships can make up the lack of structural information about such forms. Studies focused on the entropy of hydration water in CDs reveal its positioning in CD crystal, allowing to clarify the role of water in guest inclusion and corresponding phase transitions.

To make a fair comparison of solid state and solution processes, they were analyzed using a thermodynamic activity scale [1]. This approach allowed us to distinguish between the hydrophobic (solvophobic) effect and other factors affecting the stability of complexes, such as H-bonding and molecular flexibility. The latter factor is the key feature of a novel approach allowing independent theoretical calculation of binding constants.

Fast scanning calorimetry (FSC) is state-of-the-art method which allowed to find the melting points [2] and enthalpies for the natural CDs. The obtaining of such data is possible due to extremely high heating rates up to 2,400,000 K/min, opening access to study new processes which were ‘hidden’ by time in conventional methods of analysis. These data are essential for understanding the structure of liquid CDs and their comparison with aqueous solutions what reveals the structural features of water in CD solutions and answer the questions on “high-energy water” concept. Such thermodynamic analysis of CDs’ structure-property relationships in all phases facilitates optimization of guest inclusion technologies in multi-phase systems (slurries, gels) which are common for CD industry.

Acknowledgements: The work was supported by RSF and TAS grant No. 24-23-20024.

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OP35

Identification and Characterization of Mono-(6-Sulfinic Acid)-Sugammadex: A Novel Oxidative Impurity in Sugammadex Production

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Sugammadex (marketed under the brand name, Bridion®) is the first cyclodextrin (CD)-based API with a well-known mechanism of action and a result of a rational drug design and development [1,2]. Due to its structurally unique and symmetric derivatization at the primary hydroxyl positions, Sugammadex is typically produced as a single isomer. However, the complexity of its synthesis and purification processes has led to the identification of numerous related impurities, a critical concern as generic production scales up globally following patent expirations.

In our study, we report the first synthesis and detailed structural analysis of a novel impurity, mono-(6-sulfinic acid)-Sugammadex, formed via oxidative transformation of the thiol-containing side chain. This impurity has a particular importance due to the susceptibility of sulphur-containing moieties to various oxidative pathways, which can occur under the manufacturing processes.

Our work employed multi-step synthetic strategies to generate the impurity starting from γ-CD. Several synthetic routes were applied, including bromination- and sulfonylation-based transformations, followed by substitution with 3-mercaptopropionic acid and then oxidation.

The synthesized impurity was thoroughly characterized using high-resolution mass spectrometry (HRMS), 1D and 2D NMR techniques (including HSQC, COSY, HMBC), and HPLC-DAD-MS.

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OP36

Harnessing the power of β-CD-functionalized *star*-PLA for Doxorubicin delivery in Osteosarcoma cells

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Star polymers are biomaterials of growing interest in the biomedical field as powerful injectable drug delivery systems. Their exclusive structure, consisting of multiple variable-length linear chains (*arms*) radiating from a central *core,* is responsible for remarkable properties unattainable by linear polymers. [1,2]
In the framework of our studies dealing with the design of novel polymer-based Nanotherapeutics [3-5], we recently synthetized a novel three-armed *star* polylactic acid functionalized with β-CD (*star* PLA-CD) exploiting a proper combination of Ring-Opening Polymerization (ROP) of L-lactide using glycerol as the initiator, Steglish esterification and copper catalyzed 1,3-dipolar Huisgen cycloaddition (CuAAC).
The azide-alkyne Huisgen *click* reaction afforded in good yield and without side products a novel amphiphilic three-armed *star* PLA-CD copolymer able to self-assemble in water into nanoparticles and to incorporate the antitumoral drug Doxorubicin (Dox).
A sustained and prolonged drug release was promoted from *star* PLA-CD@Dox by acidic pH that stimulated nanoparticles disassembly together with DOX protonation. *In vitro* biological studies on a panel of osteosarcoma cells (U2, MG63, Saos-2, MNNG-HOS-GFP, 143B) pointed out the ability of our *star* PLA-CD@Dox nanocarriers to effectively inhibit tumoral cells proliferation, without toxicity on bone marrow derived mesenchymal stem cells (BM-MSCs), used as healthy control.

Acknowledgements: Projects PRIN 2022 (2022P99NY5) "FINE" and PRIN 2022 PNRR (P202242X25) "MERCURY".

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Flash Presentations

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FP01

Preparation of Thermosensitive Poloxamer-Based Intranasal Gel of Sulfobutylether-β-cyclodextrin and Dimethyl Fumarate Complex for the Treatment of Multiple Sclerosis

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Dimethyl fumarate (DMF), a sparingly soluble compound, is the first line FDA approved medication for treatment of multiple sclerosis. DMF is often associated with gastrointestinal adverse events, flushing, skin irritability, and in severe cases can cause progressive multifocal leukoencephalopathy [1]. The current study aimed to formulate a novel smart dosage form that not only improves the solubility and stability of DMF but also enables its intranasal administration for optimized therapeutic efficacy. Phase solubility studies were conducted using various cyclodextrins, and sulfobutylether-β-cyclodextrin (SBE-β-CD) at 10% w/v was selected for its ability to enhance the solubility of DMF by 66%. NMR analysis was performed on the individual ingredients and the DMF-SBE-β-CD binary system, confirming the inclusion complexation of the drug within cyclodextrin cavity. In the next phase, different concentrations of poloxamers (P-407, P-188) were tested to optimize the gelation temperature of the formulations within the nasal temperature range (30 – 35 °C) [2]. A formulation containing 20% w/v of P-407 and 1% w/v of P-188 was selected as it exhibited a gelation temperature of 31.0 ± 0.5 °C and a gelation time of less than 20 seconds in the inverted vial test using a water bath assembly (Figure 1). Additionally, chitosan HCl was incorporated as a mucoadhesive agent, and the optimized formulation was further characterized for its physicochemical properties.

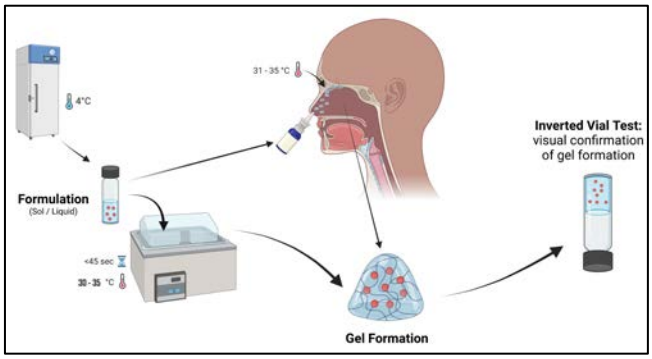

Figure 1. Graphical representation of SBE-β-CD/DMF intranasal thermosensitive gel; a transition of solution at 4 °C to gel at 31 – 35 °C.

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FP02

Self-Assembling Cationic Cyclodextrin Nanovectors: A Novel Approach for Gene Delivery

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This study presents the development of self-assembling cationic nanovectors derived from three newly modified β-cyclodextrins (CDs) synthesized by Carbohyde Srl for the complexation and transport of gene materials. Initially, the optimal method for obtaining the CDs Nanoparticles (NPs) was established, ensuring their structural integrity and functional capacity. The complexation process involved the incorporation of a plasmid (P) that expresses GFP.
To comprehensively characterize the NPs, dynamic light scattering (DLS) was employed to determine key parameters such as particle size, polydispersity index (PDI), and zeta potential both before and after siRNA complexation. Stability studies were conducted at both 4°C and 25°C, as well as in culture media. The efficiency of plasmid complexation was evaluated using gel electrophoresis, and cell viability assays were performed across different cell lines to assess the cytotoxicity of the NPs. To reduce the zeta potential and improve the "safe concentrations" of the NPs, hyaluronic acid and polysialic acid were introduced into the formulation. The results were promising, indicating that the selected NPs exhibited good stability and optimal complexation efficacy with the plasmid. Notably, the transfection capacity of the formulated nanovectors appeared highly effective, demonstrating the ability to deliver genetic material efficiently into target cells. In conclusion, stable vectors capable of complexing the plasmid and effectively transfecting cells were obtained.

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FP03

Cyclodextrin Polymers As Sorbents For The Removal Of Perfluorinated Compounds From Water

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Poly and perfluoroalkyl substances (PFAS) are compounds with remarkable properties that are widely used in industry due to their unique surface activity and stability. These compounds are characterized by a high number of carbon-fluorine (C-F) bonds. They are de-facto non-degradable in nature and because of this, they are also called "forever chemicals". The solubility of anionic PFASs in water presents a significant environmental concern, as it facilitates their entry into the food chain and potential for bioaccumulation. PFAS represent environmental and health risks, including cancer and reproductive problems. [1] Traditional water purification methods cannot effectively eliminate PFAS, and therefore alternative technologies are currently being explored, especially various sorbents. [2]

Promising solution could be cyclodextrin sorbents modified to effectively capture PFAS. Cyclodextrins are ideal hosts for hydrophobic compounds and thus can effectively trap contaminants in water. Cyclodextrin polymers have already shown potential as a sorbent for the removal of PFAS from water. [3] However, these polymers contain fluorine, which is not ideal because the introduction of other fluorinated compounds into the environment may cause additional problems. This project is focused on the preparation of insoluble non-fluorinated cyclodextrin polymers containing a positive charge or nitrogen atom. [4] For the preparation of these polymers, a narrow range of cross-linkers will be used, for example epichlorohydrin, diglycidyl ether, pyromellitic dianhydride. Different cross-linking agents will be compared in their ability to enhance binding to PFAS. Such polymers can contribute to finding an effective solution in water treatment plants to remove these hazardous substances from our environment and drinking water.

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FP04

βCD-based nanosponges vs. nigerose-based NS: piroxicam inclusion vs. adsorption and self-aggregation via molecular dynamics simulations

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β-cyclodextrins (βCDs) cross-linked with pyromellitic dianhydride (PMA) form 3D nanoporous polymers called cyclodextrin nanosponges (CDNS) able to encapsulate hydrophobic and lipophilic drugs [1]. Cyclic nigerosyl-1,6-nigerose (CNN) [2] is an interesting monomer that cross-linked with pyromellitic dianhydride form a polymer without cyclic hydrophobic cavities as shown by βCDNSs. Synthetized by Trotta et al [2] CNN is able to solubilize hydrophobic drugs for their release [2] such as PMA βCDNS as experimentally studied by Pivato et al. [3].

In the present theoretical work molecular mechanics (MM) and molecular dynamics (MD) simulations at the atomistic level [4] are performed to understand the intermolecular interactions between piroxicam — an efficient nonsteroidal anti-inflammatory agent widely used for the treatment of pain in musculoskeletal disorders — and both a PMA βCDNS and CNN. Drug encapsulation occurs only in βCD cavities in PMA βCDNS. In both cases, the drug adsorption and self-aggregation process on the surface exposed by the carrier take place. Different drug-carrier geometries of interaction and different strength of the intermolecular interactions could explain the different diffusion [4], in two steps or in single step, as found in NMR experiments [3].

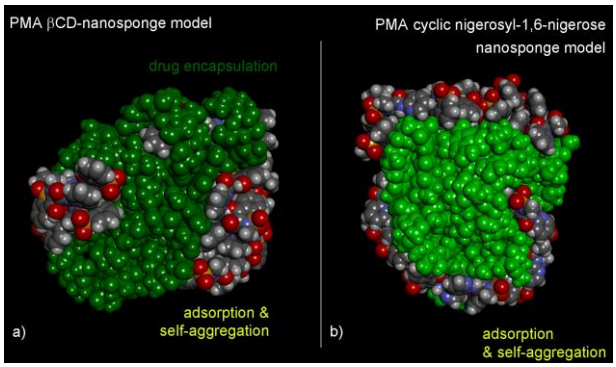

Figure 1. Optimized geometries of piroxicam adsorbed on PMA βCD-nanosponge and cyclic nigerosyl-1,6-nigerose templates after MD runs.

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FP05

Exploring THEDES–Cyclodextrin Synergy for Advanced Drug Delivery Applications

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THErapeutic Deep Eutectic Solvents (THEDES) are a novel class of green solvents formed by mixing two or more natural, pharmaceutically active components. Their low toxicity, biodegradability, and customizable properties make them promising candidates for drug delivery applications.[1] In previous publications, we demonstrated that cyclodextrins (CDs) retain their host properties in DES environment, providing genuine inclusion complexes with hydrophobic guests and API in non-aqueous media.[2,3]

This project explores a CDs-THEDES combo to create smart drug delivery systems. The synergy between the molecular encapsulation ability of CDs and the solubilizing, stabilizing, and therapeutic properties of THEDES offers a multifunctional platform for improving drug performance and delivery. Low-hydration THEDES were obtained by combining the desired active pharmaceutical ingredient (API) with selected partners (**Figure 1**). The stable formulations were added with β- and γ-cyclodextrin at different concentrations (3-10 wt%), and the resulting systems were characterized via NMR methods,[2,3] and compatibility tests with gelatin capsules.

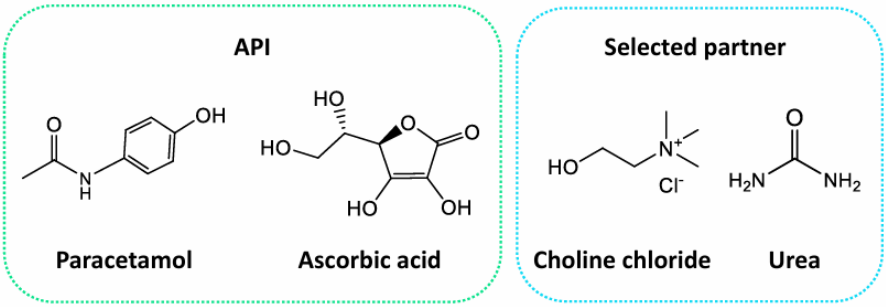

Figure 1. Structural representation of the compounds chosen for the study

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8th European Cyclodextrin Conference
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FP06

Artificially Intelligence Assisted Synthesis of Novel Cyclodextrin Derivatives

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Machine learning is being used in an expanding array of domains, with its application already extending to the prediction of the association constant between a cyclodextrin and a guest, as evidenced by the opencyclodb.org dataset [1]. Artificial intelligence (AI) also appears to be an opportunity to optimize the synthesis pathway of cyclodextrin derivatives and predict their properties. This approach is expected to bring about a transition in the field from a primarily chemical screening process to a more computational one, by means of leveraging a comprehensive analysis of experimental data. The objective is threefold: to improve the design of novel molecules, to refine the parameters of synthesis processes, and to predict the regioselectivity of syntheses.

This requires the generation of experimental data sets in synthesis and characterization to validate predictions. The aim is to accelerate access not only to new, more efficient CD derivatives, but also to less energy-intensive and more sustainable synthesis processes. All experimental data from syntheses and physico-chemical characterizations obtained on modified CDs will be systematically compiled, processed, and transformed into a format that is conducive to database integration. This format will facilitate the prediction of modified CD structures. The first results obtained on reaction etherifications are presented herein.

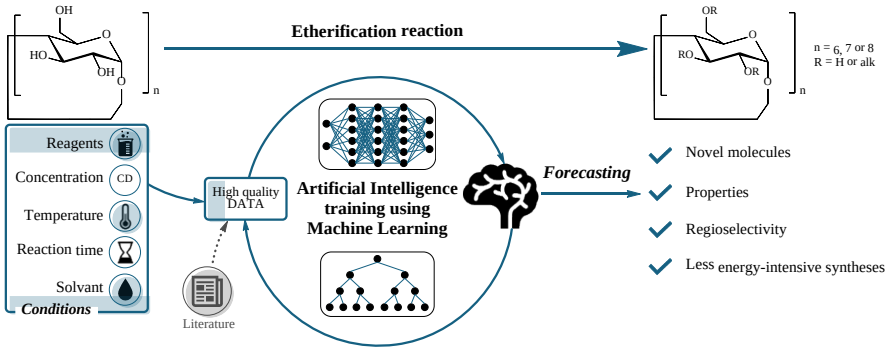

Figure 1. Schematic representation of the process of optimizing chemical reactions through the application of machine learning (ML) methodologies.

Acknowledgements: his work has benefited from the support of the National Research Agency under France 2030, MAIA Project ANR-22-EXES-0009 and “Conseil Régional des Hauts de France”.

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FP07

Exploring the interactions of β-CD/peptide inclusion complexes by *in silico* simulations

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β-cyclodextrin (β-CD) inclusion complexes are a class of supramolecular systems used in various fields that are held together through non-covalent interactions between β-CD and a guest. The β-CD hydrophobic cavity encapsulates a variety of molecules, going from small organic compounds to the side chains of larger biologically active substances. The ability of β-CDs to form inclusion complexes enhances the solubility, stability, and bioavailability of the guest molecules [1].

When the guest is a peptide, the CDs form inclusion complexes with its hydrophobic parts. In this context, in silico simulations, such as Molecular Dynamic (MD), provide detailed insights into the characteristics of these compounds exploring the conformational changes that may occur to the secondary structure of the peptide upon complex formation [2]. By simulating, we can predict the molecular details of the inclusion process and the solvent influence. Moreover, MD simulations can help in the design of the complexes prior to experimental analysis, by revealing how modifications could improve guest encapsulation.

Here, we show in silico simulations performed on different systems: five model pentapeptide/β-CD complexes and a bio-mimetic peptide. In the first case, the docked structures of the models were validated by MD, while for the second system free simulations in explicit water were run.

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FP08

Quaternary Ammonium-Bridged Cyclodextrins Capable of Self-Assembling into Linear Nanostructures in Water

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First described in 1990's, supramolecular polymers (SMPs) have given rise to a rich chemistry over the years thanks to the many non-covalent bonds or weakly-binding interactions available for constructing increasingly sophisticated and diverse nanostructures. This development has in turn paved the way for the emergence of materials with unique properties ranging from self-healing materials to biocompatible and bioactive polymeric materials. [1] Amongst the various non-covalent interactions, those involving the inclusion of a guest molecule within a host hold a prominent position in the field of SMPs, particularly when the host is biocompatible and environmentally benign, as in the case of the naturally occurring cyclodextrins (CDs). [2], [3], [4] In this communication, we report a highly diastereoselective synthesis of cationic permethylated α- and β-cyclodextrins (α-CDs and β-CDs), incorporating a quaternary ammonium unit bridging two adjacent glucose units. This novel methodology provides access to amphiphilic α-CDs equipped with an outward-facing alkyl chain (Figure 1), which self-assemble in water to form linear, head-to-tail supramolecular oligomers (DP up to 5 CD units) when the alkyl chain is sufficiently short (C8 and C12), and micellar structures with a longer C16 chain. Alternatively, permethylated β-CD analogs bearing an adamantyl unit have also been prepared and the fixed stereochemistry of the quaternary ammonium nitrogen and the blocked narrow opening of the CD, these amphiphilic cationic host molecules are prevented from undergoing self-inclusion or forming head-to-head dimers in water.

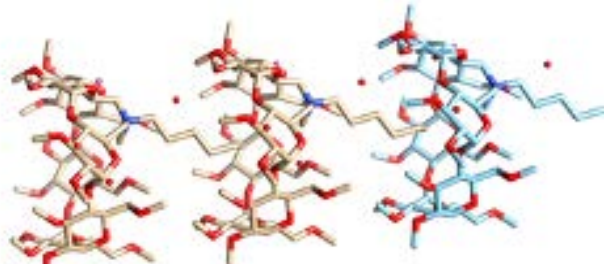

Figure 1. Molecular structure of a cationic cyclodextrin equipped with an outward-facing hexyl chain showing head-to-tail stacking of amphiphilic CDs in the solid.

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FP09

Development of Cationic β-Cyclodextrin Nanosponges for siRNA Delivery in Caco-2 Cells: A Targeted Gene Silencing Approach

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In recent years, significant research efforts have been focused on the development of cross-linked β-cyclodextrins for drug delivery and controlled release applications. In addition, cationic nanosponges have shown promise in gene delivery due to their high stability, low immunogenicity, and efficient nucleic acid encapsulation. Their ability to form stable complexes with negatively charged biomolecules, such as siRNA, makes them attractive candidates for therapeutic applications[1]. Caco-2 cells are widely used as an *in vitro* model for intestinal epithelial barriers, which are important for the study of gastrointestinal diseases, including colorectal cancer and crohn's disease. Epithelial cell adhesion molecule (EpCAM) is overexpressed in colorectal cancer and plays an important role in tumor progression, making it a potential therapeutic target for RNA-based gene silencing strategies[2]. In this study, novel cationic β-cyclodextrin-based nanosponges were developed as a delivery system for EpCAM-targeted siRNA to improve gene therapy outcomes. The key features of these nanosponges include small particle size, high stability, low toxicity, and controlled release capability. The design strategy involved the covalent binding of β-cyclodextrin with cationic molecules to increase the efficiency of siRNA complexation while incorporating polyethylene glycol (PEG) chains to improve stability and minimize aggregation.The physiochemical characterization of the synthesized cationic nanosponges included thermogravimetric analysis (TGA), spectroscopic techniques (FTIR and ^{1}H NMR), and elemental analysis (CHNS). These analyses confirmed successful cross-linking and PEG conjugation, with CHNS further confirming the presence of nitrogen groups, indicating successful conjugation of cationic molecules. When combined with siRNA, dynamic light scattering (DLS) measurements showed favorable particle sizes (70–107 nm) and positive zeta potentials (+21 to +28mV), confirming the stable formulations, while agarose gel electrophoresis confirmed efficient siRNA encapsulation.Cell viability assays (CellTiter-Fluor) showed good biocompatibility of the synthesized cationic nanosponges after 48 hours in undifferentiated Caco-2 cells. Transfection experiments showed that siRNA/nanosponge (siRNA/NS) led to a significant reduction in EpCAM expression (up to 50%) after 48 hours, indicating efficient siRNA delivery. In addition, cellular uptake studies using Cy5®-labeled siRNA confirmed efficient internalization in undifferentiated Caco-2 cells within 6 hours as determined by fluorescence-activated cell sorting (FACS) analysis. These results emphasize the potential of cationic β-cyclodextrin-based nanosponges as a promising RNA delivery platform.

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FP10

Supramolecular UV-curable Hydrogels without Photo-initiator for 3D Bioprinting

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Supramolecular hydrogels represent three-dimensional hydrophilic polymer networks that can absorb and retain substantial volumes of water. The reversible physical bonds connecting the chains impart viscoelastic properties to the hydrogels. In the present study, self-healing, shear-thinning, and UV-curable hydrogels were synthesized by forming inclusion complexes between cyclodextrin (CD) host molecules and benzophenone and/or adamantane guest molecules. The inclusion complex established between CD and benzophenone facilitates the formation of covalent bonds upon exposure to UV irradiation, eliminating the necessity for photo-initiators and developing robust hydrogels.[1, 2] Furthermore, this research aims to evaluate these innovative hydrogel materials' physicochemical and biological properties for 3D bioprinting, showing good printability and durability. The chemical structures of the modified dextran were validated by the characteristic peaks observed in the NMR and FT-IR spectra. The material exhibited dynamic rheological properties, which could be efficiently adjusted by varying the anchor point ratio, the chain length of the dextran backbone, the solution concentration, and the hydrogel composition. In vitro assays demonstrated that the hydrogel's cytotoxicity was negligible. The satisfactory printability of the hydrogel has been demonstrated through tests conducted with a bioprinter. Unlike GelMA, no temperature control is required during printing. The hydrogel can be completely cured into a solid state through 365 nm ultraviolet treatment for merely 10 seconds. These hydrogels demonstrate significant potential for bioprinting applications within tissue engineering.

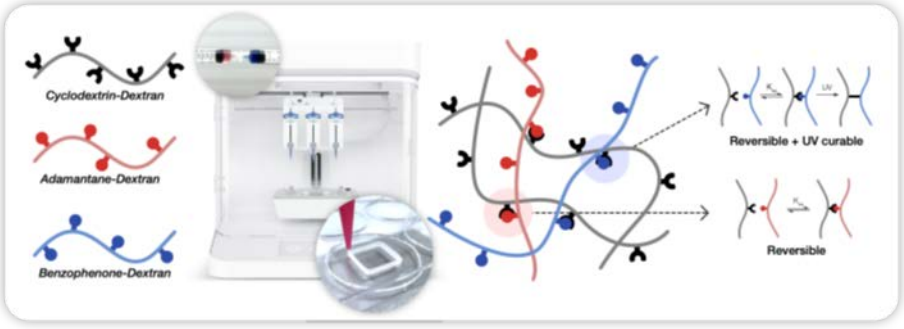

Figure 1. Graphical representation of hydrogel structure and 3D bioprinting.

Acknowledgments
This project is supported by a grant from the Independent Research Fund Denmark (nr. 2035-00275B).

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FP11

Surface modification of cotton fabric for adsorption of essential oils

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The main objective of this work was to obtain a cotton fabric modified by grafting β-cyclodextrin (β-CD) in order to retain essential oil fragrances. The grafting of β-CD on the fabric was confirmed by FTIR-ATR due to the appearance of a band at 1728 cm^{-1}, the carbonyl signal, corresponding to the formation of the ester bond between the cellulose of the fabric and β-CD, mediated by a polycarboxylic acid 1,2,3,4-butanetetracarboxylic acid (BTCA), which took part in the condensation reaction. The indirect spectrophotometric method using phenolphthalein as a probe was used to quantify that 1.7±0.5 μmol of β-CD were grafted per gram of cotton fabric. Orange and cinnamon oils were adsorbed on the cotton fabric and their retention was determined over 15 days in atmospheric air using gas chromatography-mass spectrometry (GC-MS) analysis. It was found that the β-CD modified fabric did not prolong the retention of the essential oils over time, but promoted a significant increase in the initial amount of D-limonene (150%) for orange oil and cinnamaldehyde (280%) for cinnamon oil. The data suggest that adsorption can occur in two ways: 1) encapsulation of the molecule in the cavity of β-CD or 2) physical adsorption on the cellulose surface by hydrogen bonding. The carbonyl bond of the aldehyde group present in the cinnamaldehyde molecule is prone to interact with the cellulose structure and the aromatic ring is able to form an inclusion complex with β-CD. On the other hand, the absence of polar groups in the D-limonene molecule contributed to the formation of the inclusion complex with β-CD. Figure 1 summarizes and illustrates these possible interactions of the main components of the essential oils with the modified fabric.

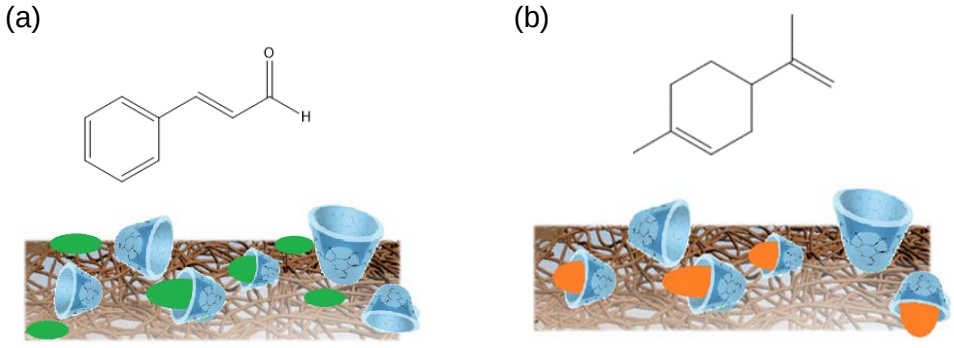

Figure 1. Illustration of the interaction of cinnamaldehyde (a) and D-limonene (b) on cotton fabric modified by grafting β-cyclodextrin.

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FP12

Complexation of citalopram with β-cyclodextrin, mono-subetadex and subetadex: phase solubility, Hummel-Dreyer, ACE, ITC and NMR studies

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Cyclodextrins (CDs) have a number of important properties, such as chiral separation or the enhancing of water solubility of various substances. In the present study the complexation properties of sugammadex analogue CDs, such as subetadex (SBX) and mono-subetadex (monoSBX) was investigated and compared with the native β-CD. These CDs are isomerically pure, persubstituted or monosubstituted with carboxythioether groups on the primary side. The structure and properties of these CDs can be determined more easily and accurately than in case of randomly substituted CDs.

The complexation features are investigated at pH 7.4 using citalopram, a selective serotonin reuptake inhibitor antidepressant, as a model compound. The stability constant was comprehensively investigated by different methods (phase-solubility test, Hummel-Dreyer method (HD method), affinity capillary electrophoresis (ACE), and ITC). The ^{1}H NMR studies supported the results from the investigated techniques and the complex structure characterized by ROESY NMR studies. Our aim was to gain a deep understanding of the complex structure that forms between SBX or monoSBX and citalopram, and to compare the stability constants obtained by these techniques.

The phase solubility study gave different results from the other three techniques, with monoSBX showing the highest stability constant. In case of HD method, the stability constants differed significantly from those of the ACE and ITC methods, but the trend in CD stability followed the same order (β-CD < monoSBX < SBX). The ACE and ITC methods gave very similar results for β-CD and monoSBX, with some deviations for SBX, although still within the same order of magnitude. Based on the results, ACE and ITC are the most reliable techniques for determining CD-guest stability constants.

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FP13

Synthesis of CD-derivatives for photoinduced therapeutic regimes bypassing hypoxia

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Hypoxia is a condition characterized by low concentrations of molecular oxygen in poorly vascularized tissues, which occurs, among other diseases, in solid tumours and microbial or fungal infections. In such hypoxic regions, the efficacy of both drug-based and photo-induced therapies is significantly reduced, thus restoring optimal oxygen levels is a primary goal to improve treatment outcomes. A promising strategy is to combine well-established drugs (i.e. chemotherapeutics, antimicrobial agents and photosensitizers) with aromatic endoperoxides, which act as oxygen releasing agents (ORAs). In this frame, we synthesized 9,10-disubstituted anthracenes able to reversibly bind and release oxygen upon thermolysis in physiologically compatible conditions, thereby restoring optimal oxygen levels in hypoxic environments.[1] Noticeably, the endoperoxide preparation was optimized under flow conditions in homogeneous aqueous environment.[2] We will present the first results on the synthesis of cyclodextrin-based derivatives functionalised with disubstituted anthracenes and photosensitizers, with the ultimate goal of developing an optimized platform capable of delivering simultaneously three different therapeutical agents for the treatment of cancer or microbial infections. To achieve the three-component synergistic therapeutic effect, we investigated various strategies involving both covalent conjugation and supramolecular loading onto a cyclodextrin-based platform, with emphasis both on its synthesis and therapeutic performance.

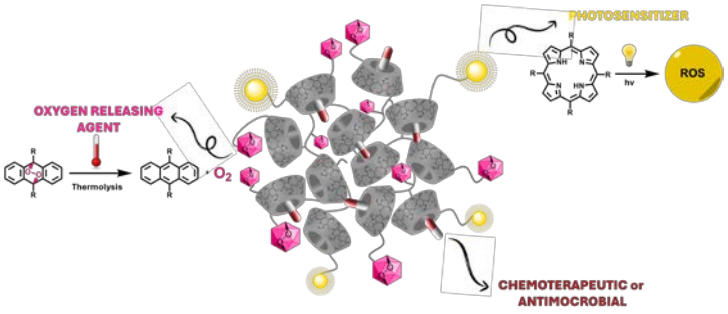

Figure 1. Schematic representation of a cyclodextrin-based platform able to carry contemporarily ORAs, photosensitizers and chemotherapeutical or antimicrobial drug.

Acknowledgements: This project has received funding from the European Union's Horizon Europe research and innovation programme under the Marie Sklodowska-Curie grant agreement Bicyclos N°101130235.

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FP14

Advantages in the use of Cyclodextrins for paediatric oral formulations

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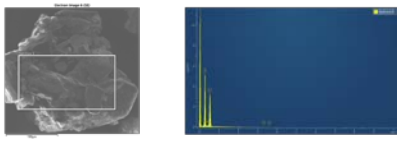
Cyclodextrins are excipients known for their ability to form inclusion complexes with hydrophobic components. Their application in pharmaceutical formulations offers several advantages, particularly relevant in the development of oral pediatric medications [1]. Treating pediatric patients presents significant challenges due to the limited availability of age-appropriate dosage forms, lack in clinical studies involving children and difficulty of administration [2]. The careful selection of excipients is crucial, as substances usually used in adult dosage form are potentially harmful for pediatric formulations. Cyclodextrins, owing to their favorable safety profile and functional properties, can represent promising candidates for this purpose, however, their use in pediatric formulations is limited by the existence of an established acceptable daily intake (ADI). Maltodextrins, which exhibit comparable functional properties, are considered a more favorable alternative as no ADI restrictions are currently associated with their intake [3]. This study aims to develop a pediatric oral formulation containing paracetamol by exploiting the ability of cyclodextrins and maltodextrins to encapsulate the active pharmaceutical ingredient (API), followed by characterization of the resulting pharmaceutical product. As liquid oral form could be exposed to instability due to bacterial attacks, harmful chemical reactions and reduced shelf life [4], oral granulates were identified as the preferrable dosage form, offering stability, ease of administration, improved patient compliance, fast dissolution profile and favorable rheological properties. The wet granulation was selected as a suitable process for both laboratory-scale production and industrial-scale application. The formation of the complex was investigated through dissolution studies and scanning electron microscopy images (FE-SEM), confirming the compatibility, processability and scalability of the selected components. Rheological assessments were evaluated to estimate final pharmaceutical properties, providing good flowability and compressibility index (AoR <40°, Carr's Index 1-10%). Future in vivo studies are expected to further elucidate the pharmacokinetic and pharmacodynamic properties of these systems, supporting the broader application of cyclodextrin and maltodextrins-based formulations in pediatric drug development.



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Spectrum 6	54.54	2.44	42.13	0.89	100.00

Figure 1. EDS analysis with FE-SEM microscope showing granulates chemical composition

Acknowledgements: Special thanks to Roquette Italia Spa for providing cyclodextrins and maltodextrins used in this study

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FP15

Hydroxypropyl-β-Cyclodextrin-Assisted Freeze-Drying: A Strategy to Improve the Stability of Cannabis Nanoemulsions

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Nanoemulsions (NEs) are advanced colloidal systems designed for the delivery of lipophilic active compounds, such as phytocannabinoids found in *Cannabis* oil extracts[1,2]. However, their long-term stability is limited by susceptibility to oxidation and by droplet aggregation and coalescence. Freeze-drying, combined with the use of cryoprotectants, emerges as an effective strategy to overcome these limits, preserving the structural integrity of the formulations and improving patient compliance through enhanced storage and transportability**.**

In this study, a NE was developed containing *Cannabis Bedrocan*® extract in MCT oil (medium-chain triglycerides, 50% w/w), stabilized with non-ionic surfactants[1]. Freeze drying studies were carried out with the aim of obtaining a dry powder, to be reconstituted prior to use, in order to improve the stability of the formulation without altering its key properties, such as droplet size and drug content. Comparative studies were conducted to evaluate the effectiveness of different cryoprotectants, such as mannitol and hydroxypropyl-β-cyclodextrin (HPβCD). The results demonstrated a clear superiority of HPβCD over mannitol in protecting the NE during freeze-drying. Following the identification of HPβCD as the most effective cryoprotectant, its concentration (w/w %) was optimized to maximize formulation stability. The data showed that HPβCD not only prevents particle coalescence during the freeze-drying process but also significantly reduces droplet size upon redispersion in water compared to the untreated NE. In particular, a concentration of 10% was found to be optimal, ensuring a greater reduction in size while preserving the structural integrity of the NE. The beneficial effects are attributed to the ability of HPβCD to form inclusion complexes with hydrophobic molecules, thereby preventing droplet aggregation during freezing and drying. In addition, HPβCD protects labile molecules against oxidative degradation and photodegradation[3], offering an additional advantage for the stabilization of Cannabis-based NEs.

These results suggest that the optimized use of HPβCD as a cryoprotectant not only enhances the stability of *Cannabis*-based NEs but also paves the way for the development of safer, more stable, and patient-friendly formulations.

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Resveratrol-4'-DHA encapsulation in HP-beta-cyclodextrins

FP16

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The poor aqueous solubility of many bioactive compounds continues to pose significant challenges in pharmaceutical and biomedical applications. Resveratrol-4'-DHA (Resv-DHA), an ester derivative formed through the conjugation of resveratrol with docosahexaenoic acid (DHA) at the 4'-hydroxyl position, exhibits improved antioxidant and bioactive properties compared to its parent compound [1]. In this study, we investigated the solubilization of Resv-4'-DHA and DHA by complexation with 2-hydroxypropyl-β-cyclodextrin (HP-β-CD).

Critical micellar concentration (CMC) and complexation constants were determined using fluorescence spectroscopy, employing the method of Chattopadhyay et al. (1984) [2]. Solutions containing increasing concentrations of HP-β-CDs in 100 mM PBS (pH 7.0) were supplemented with Resv-DHA or DHA, and DPHT (in THF) was used as a fluorescent probe. Samples were vortexed and equilibrated at 35°C for 60 minutes in the dark prior to fluorescence measurements.

Our findings indicated that Resv-4'-DHA formed micelles at lower concentrations than DHA, suggesting enhanced self-assembly behavior. The presence of HP-β-CDs increased the CMC for both compounds, reflecting that the complexation of them in the hydrophobic cavity of CDs implies an increase in the water solubility of them. Complexation analysis revealed differing stoichiometries: DHA formed 1:1 inclusion complexes, whereas Resv-DHA formed 1:2 complexes with HP-β-CDs.

These results contribute to the understanding of solubilisation mechanisms for lipophilic bioactives and support the use of HP-β-CDs as complementary strategies to enhance bioavailability of Resv-DHA.

Acknowledgements: This work was carried out as part of the project LIPOFOOD (PID2020-120466RB-I00 Spanish Ministry of Sci. e Innovación) and 22015/PI/22 (Fundación Séneca de la Región de Murcia), and was carried out as part of the predoctoral contract funded by Fundación Séneca Región de Murcia (Spain) 21794/FPI/22.

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FP17

Host-guest complexes based on Cyclodextrins and a pyranoflavylium-type dye for capturing biogenic amines

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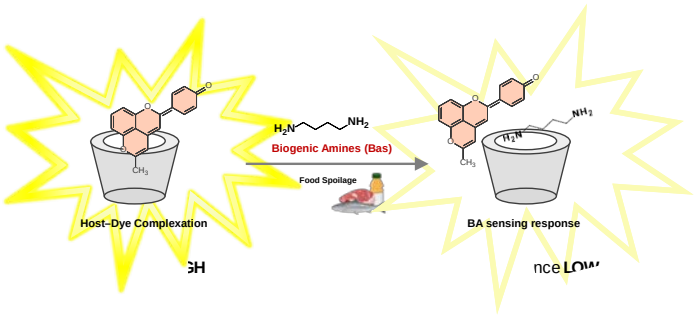
Biogenic amines (BAs) are nitrogenous compounds that behave as crucial markers for food spoilage, demanding the development of rapid, selective, and sensitive detection method[1]. The main goal of this work was the development of a colorimetric host-guest molecular switch based on interactions between a bioinspired 10-methylpyrano-4'-hydroxyflavylium[2[guest dye and the cyclodextrin derivatives host with sensing ability for biogenic amines.

Four β-CD derivatives were used to investigate their supramolecular interactions with PyFlav compound: native β-CD, two sulphobutylether-functionalized β-CDs (with substitution degrees (DS) of 4 and 7, and a carboxymethyl-modified β-CD with a DS of 3.5. These systems were characterized using UV-Vis and fluorescence spectroscopy, revealing an association constant (Kass) around 10^3 with a slight bathochromic shift and a great enhancement in the fluorescence intensity. The complexation of the pigment did not lead to a significant change in the pKa value; however, a bathochromic shift was observed, with the quinoidal base species transitioning from orange to pink. The sensing activity of seven BAs (putrescine, tyramine, histamine, spermine, spermidine, 2-phenylethylamine, and cadaverine) was studied by fluorescence spectroscopy. An enhancement in the presence of the hosts was seen, followed by the fluorescence quenching of the dye:β-cyclodextrin system with increasing additions of BAs. The fluorescence response was found to be selective depending on the structural nature of the BAs and on the structural difference of the hosts in the study.



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FP18

Small Ring – Big impact

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How will cyclodextrins influence our future?

Cyclodextrins, once a niche topic of academic curiosity, have grown into versatile enablers of innovation across multiple sectors. While their pharmaceutical applications are well-documented, this presentation will highlight a series of case studies that trace the journey of cyclodextrin-based technologies from academic research to market success in non-pharmaceutical industries such as cosmetics, food, and environmental protection.

Each case study will explore the critical turning points—both scientific and strategic—that influenced the innovation path, including formulation challenges, regulatory considerations, scale-up limitations, and market positioning. The presentation will examine the broader industrial and economic contexts that shape the development of new technologies, with special attention to collaboration models, intellectual property strategies, and the role of industry-specific demands.

By analyzing real-world examples, the talk will provide insights into what makes a cyclodextrin-based innovation not only scientifically viable but also commercially sustainable. The goal is to foster discussion around how academic research can more effectively align with industrial needs to accelerate technology transfer and value creation.

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Poster Session

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PP01

Development of Imatinib/Cyclodextrin Complex-Loaded Niosomes for Lung Cancer Therapy

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Lung cancer is a leading cause of cancer-related mortality worldwide [1]. Non-small cell lung cancer, a heterogeneous type of tumours, represents approximately 85% of all lung cancer cases, and occurs almost exclusively in smokers [2]. Effective cancer treatment aims to deliver drugs that specifically target cancer cells at the optimal dose. Imatinib (IMB), a selective kinase inhibitor, has been shown therapeutic efficacy against the lung cancer and the inhibition concentration at 50% (IC_{50}) on A549 cell growth is at the range of 2–3 μM [3]. However, its application is often limited due to its low aqueous solubility [4,5]. This study investigated the formation of water-soluble IMB/cyclodextrin (CD) inclusion complexes. IMB demonstrated a high affinity for γCD and HPγCD, as evidenced by phase-solubility studies, solid- and solution-state characterizations, and molecular docking study. IMB/CD-loaded niosomes in the presence and absence of D-alpha-tocopheryl polyethylene glycol succinate (TPGS) were prepared using thin-film hydration method [6]. The developed niosomal formulations were characterized in terms of particle size, size distribution, zeta potential, and entrapment efficiency (%EE). These niosomal formulations were shown in nanosized and spherical structure with high %EE. The novel IMB/CD-loaded niosomes comprised with TPGS showed significantly increased in cytotoxic activity (IC_{50} value; 5 μM) and cellular uptake to the A549 lung cancer cell line. IMB-loaded niosomal formulations, particularly IMB/HPγCD-loaded niosomes in the presence of TPGS significantly enhance the efficacy of IMB in inducing apoptotic cell death in lung cancer cells. These results indicate that our developed IMB/CD-loaded niosomes could be a promising for effective delivery of IMB into lung cancer cells and paving the way for clinical lung cancer therapy.

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PP02

βCD-based nanosponges vs. nigerose-based NS: piroxicam inclusion vs. adsorption and self-aggregation via molecular dynamics simulations

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β-cyclodextrins (βCDs) cross-linked with pyromellitic dianhydride (PMA) form 3D nanoporous polymers called cyclodextrin nanosponges (CDNS) able to encapsulate hydrophobic and lipophilic drugs [1]. Cyclic nigerosyl-1,6-nigerose (CNN) [2] is an interesting monomer that cross-linked with pyromellitic dianhydride form a polymer without cyclic hydrophobic cavities as shown by βCDNSs. Synthetized by Trotta et al [2] CNN is able to solubilize hydrophobic drugs for their release [2] such as PMA βCDNS as experimentally studied by Pivato et al. [3].

In the present theoretical work molecular mechanics (MM) and molecular dynamics (MD) simulations at the atomistic level [4] are performed to understand the intermolecular interactions between piroxicam — an efficient nonsteroidal anti-inflammatory agent widely used for the treatment of pain in musculoskeletal disorders — and both a PMA βCDNS and CNN. Drug encapsulation occurs only in βCD cavities in PMA βCDNS. In both cases, the drug adsorption and self-aggregation process on the surface exposed by the carrier take place. Different drug-carrier geometries of interaction and different strength of the intermolecular interactions could explain the different diffusion [4], in two steps or in single step, as found in NMR experiments [3].

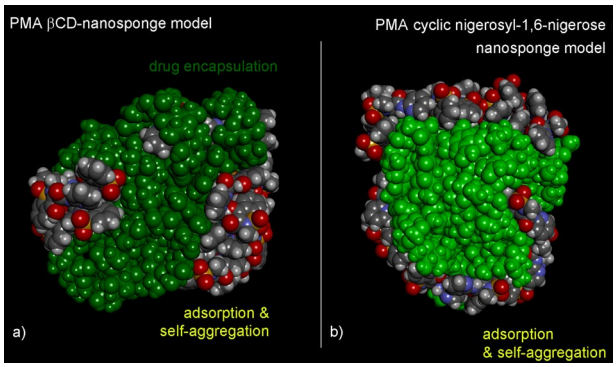

Figure 1. Optimized geometries of piroxicam adsorbed on PMA βCD-nanosponge and cyclic nigerosyl-1,6-nigerose templates after MD runs.

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PP03

Cyclodextrin Ophthalmic hydrogel for the treatment of corneal injuries

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Approximately 3% of all emergency department visits are due to eye trauma, most of which are corneal injuries, including those caused by corneal abrasions or foreign bodies. Tipically, Vitamin B12 eye drops are administered in conjunction with an antinfection agent. Vitamin B12 has been shown to enhance the process of re-epithelialisation of the corneal epithelium and to reduce stromal oedema. Numerous studies with the enzyme Q10 have shown that it reduces ocular hyperaemia, preserves mitochondrial function and promotes epithelial re-epithelialisation. Idebenone is a synthetic analogue of CoQ10, whose function is to scavenge reactive oxygen species (ROS). The objective of this study is to develop a hydrogel containing Vitamin B12 and Idebenone for use as a complementary treatment to promote the re-epithelialisation of damaged corneas.To prepare the hydrogels, a 20% (w/v) aqueous solution of hydroxypropyl-β-cyclodextrin (HPβCD) was prepared. Next, Idebenone (10 mg/mL) and Hydroxocobalamin (5 mg/mL) were added and subjected to magnetic stirring until completely dissolved. Subsequently, 15 % (w/v) poloxamer 407 (FP) was added to formulate a thermosensitive hydrogel. The hydrogel was characterized by pH and viscosity. The inclusion complexes among HPβCD, drugs and poloxamer 407 were studied by nuclear magnetic resonance (NMR). In addition, the release profile of both drugs was evaluated by *in vitro* release study. The ocular toxicity and security were evaluated by different tests: Hen´s Egg Test on the Chorioallantoic Membrane (HET-CAM), Bovine Corneal Opacity and Permeability Test (BCOP), viability in corneal epithelial cells and *C. elegans* survival. NMR data showed that Hydroxocobalamin, Idebenone and Poloxamer exhibit affinity and interactions with HPβCD. Ocular irritation studies conducted on bovine corneas (BCOP) and chorioallantoic membrane (HET-CAM) demonstrated the safety of the formulation. According to data obtained in the corneal epithelial cell viability assay, FP at 200 µM reduced cell viability in epithelial cells by up to 50%. However, FP at 50 µM in terms of Idebenone maintained cell viability above 77%. Testing in *C. elegans*, an animal model with signalling pathways similar to those found in humans, demonstrated the safety of hydrogel at 200 µM in terms of Idebenone. Toxicity tests concluded that the formulation is safe and suitable for treatment of corneal injuries.

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PP04

Removal capacity of different micropollutants by polypropylene coated with amphiphilic cyclodextrins

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The presence of organic micropollutants in water like pharmaceuticals and pesticides are of great concern due to the potential health effects to living organisms. Cyclodextrin based technologies are promising adsorbents for the removal of micropollutants [1]. An easy and fast method to modify polymeric materials with cyclodextrins, to increase their removal capacity of micropollutants, rely on the self-assembly properties of amphiphilic cyclodextrins (ACDs). This method has earlier been used to modify the polymeric material polypropylene for the removal of volatile organic compounds [2]. The aim of this study is to investigate how the degree of substation (DS) of the ACDs and the properties of the micropollutants affect the removal capacity by polypropylene coated with ACDs.

Non-woven polypropylene was coated with ACDs with varying DS by dip coating in a mixture of ACD, ethanol and water. The removal capacity of each micropollutant was determined in static adsorption experiments with the same initial molar concentration of micropollutant in water.

The static adsorption experiments demonstrated that the removal capacity of the ACD coated polypropylene both depends on the DS of the ACD and the properties of the micropollutant.

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PP05

Artificially Intelligence Assisted Synthesis of Novel Cyclodextrin Derivatives

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Machine learning is being used in an expanding array of domains, with its application already extending to the prediction of the association constant between a cyclodextrin and a guest, as evidenced by the opencyclodb.org dataset [1,2]. Artificial intelligence (AI) also appears to be an opportunity to optimize the synthesis pathway of cyclodextrin derivatives and predict their properties.

This approach is expected to bring about a transition in the field from a primarily chemical screening process to a more computational one, by means of leveraging a comprehensive analysis of experimental data. The objective is threefold: to improve the design of novel molecules, to refine the parameters of synthesis processes, and to predict the regioselectivity of syntheses.

This requires the generation of experimental data sets in synthesis and characterization to validate predictions. The aim is to accelerate access not only to new, more efficient CD derivatives, but also to less energy-intensive and more sustainable synthesis processes. All experimental data from syntheses and physico-chemical characterizations obtained on modified CDs will be systematically compiled, processed, and transformed into a format that is conducive to database integration. This format will facilitate the prediction of modified CD structures. The first results obtained on reaction etherifications are presented herein.

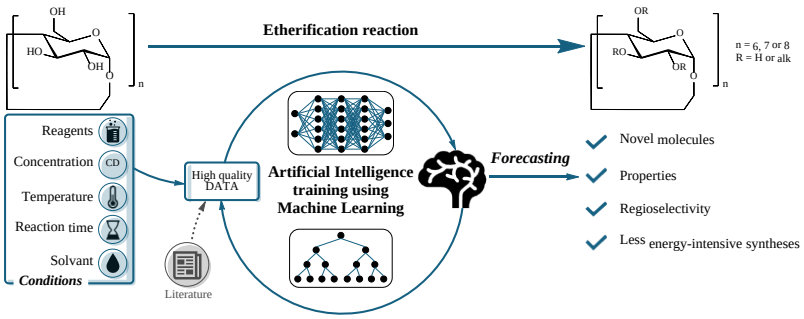

Figure 1. Schematic representation of the process of optimizing chemical reactions through the application of machine learning (ML) methodologies.

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PP06

The Preparation of Positively Charged Cyclodextrin Sorbents for PFAS Removal

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Per- and polyfluoroalkyl substances (PFAS) are persistent environmental pollutants that pose serious risks to human health and ecosystems. Due to their chemical stability and bioaccumulation potential, PFAS contamination has become a global concern, necessitating the development of effective remediation strategies. In response to this challenge, we present an innovative sorbent based on a substituted cyclodextrin, specifically designed to enhance PFAS adsorption efficiency through positive surface charge interactions.

The developed sorbent consists of β-cyclodextrin functionalized with N,N,N'-trimethylethylenediamine and crosslinked using pyromellitic dianhydride (PMDA). The material was extensively characterized to confirm its structure and properties. Nuclear Magnetic Resonance (NMR) spectroscopy was employed to verify the successful functionalization and determine the degree of crosslinking. Fourier-transform infrared (FTIR) spectroscopy confirmed the bonding between cyclodextrin and the crosslinking agent, while scanning electron microscopy (SEM) provided insight into the sorbent's morphology and surface characteristics.

The adsorption performance of this novel sorbent towards various PFAS compounds will be investigated, and the results will be presented at the conference. These findings will contribute to the development of more efficient sorbents for PFAS removal, offering a promising approach for mitigating contamination in water treatment applications.

Acknowledgements: This work was supported by the Student Grant Competition of the Technical University of Liberec under the project No. SGS-2024-4440.

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PP07

Sertraline solubilization by cyclodextrins to replace ethanol in pediatric oral solution

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Currently, pediatric sertraline HCl (anti-depression drug) commercial oral liquid formulation is using ethanol as a solvent. In our study, we screened native β-cyclodextrin and its hydroxypropylated and methylated derivatives as solubilizers to replace EtOH. Sertraline HCl is a BCS Class II drug with 0.890 mg/mL water solubility, 5.15 log P, 9.56 pKa, is marketed as tablets (25 mg, 50 mg, and 100 mg), capsules (100 mg and 200 mg), and oral ethanol solution (20 mg/mL). Higuchi and Connors method was used to screen solubilization potential of KLEPTOSE® (β-cyclodextrin), KLEPTOSE® HP (hydroxypropyl β-cyclodextrin), KLEPTOSE® HPB (hydroxypropyl β-cyclodextrin), and KLEPTOSE® CRYSMEB (methylated cyclodextrin) for this API. Phase solubility was evaluated by high performance liquid chromatography (HPLC), and complex formation by differential scanning calorimetry (DSC) and X-ray diffraction (XRD). Stability constant and complexation efficiency were calculated using phase solubility diagrams. Sertraline solubility increase by complex formation can be ranked as 300 mM KLEPTOSE® HPB (23.54 mg/mL)> 200 mM KLEPTOSE® HP (14.68 mg/mL)> 176 mM KLEPTOSE® CRYSMEB (14.01 mg/mL)> 14 mM KLEPTOSE® (2.06 mg/mL).

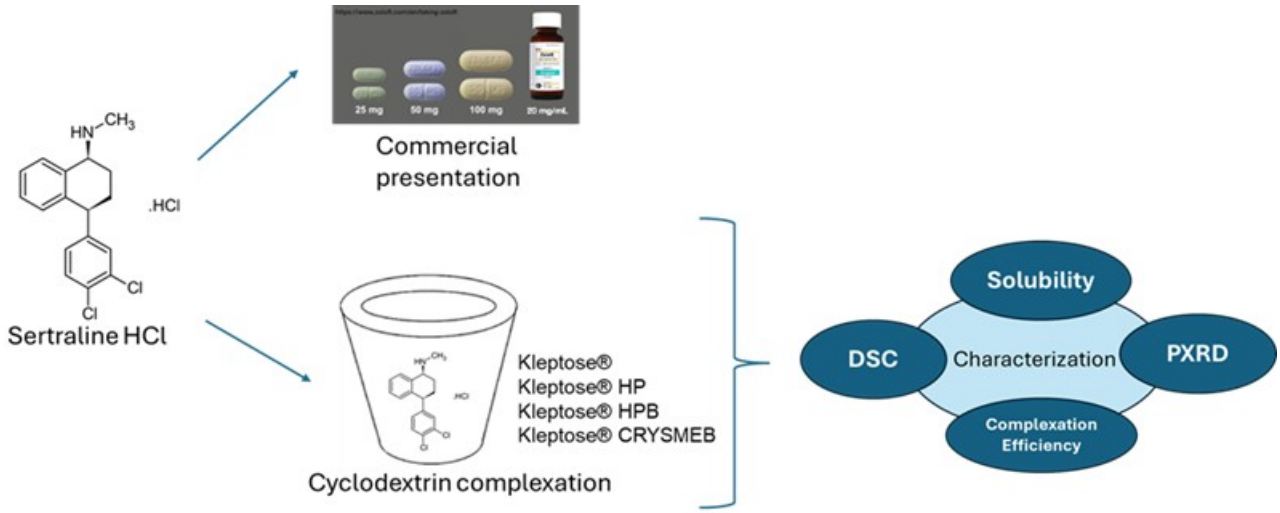

Figure 1. Graphical abstract of sertraline HCl solubilization with cyclodextrins.

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PP08

BCS Class II drugs solubilized with hydroxypropyl β cyclodextrin derivatives as oral liquid dosage form

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In order to improve patient compliance, for commercially available solid dosage form of BCS Class II drugs, apixaban and tafamidis meglumine, we developed an oral liquid dosage form using KLEPTOSE® hydroxypropyl β-cyclodextrin derivatives (hydroxypropylated and methylated β-cyclodextrin) as solubilizer. Saturation solubility of apixaban and tafamidis meglumine was evaluated based on the phase solubility technique developed by Higuchi and Connors, under supersaturated conditions. Samples were filtered through 0.22 µm PTFE filter and evaluated by high performance liquid chromatography (HPLC). Also, to prove complex formation, filtrates were lyophilized using lyophilizer (Freezone 2.5 Plus, Labconco®, Kansas City, MO) and evaluated by differential scanning calorimetry (DSC) and X-ray diffraction (XRD).

Tafamidis meglumine solubility increased by complex formation, compared with its water solubility, with 300 mM KLEPTOSE® HPB hydroxypropyl β-cyclodextrin and 150 mM KLEPTOSE® CRYSMEB methylated β-cyclodextrin by 63 times and 80 times, respectively. In the case of apixaban, solubility increased, relative to its water solubility, 307 times and 294 times in 300 mM HPB and 150 mM CRSMEB, respectively. Both APIs showed complex formation with KLEPTOSE® HPB and KLEPTOSE® CRYSMEB. APIs endothermic peak is at 238.63 °C (apixaban) and 198.20 °C (tafamidis meglumine). DSC thermogram of apixaban and tafamidis meglumine cyclodextrin complex did not show endothermic peak of API, illustrating complete complexation of APIs with both cyclodextrins, also confirmed by XRD.

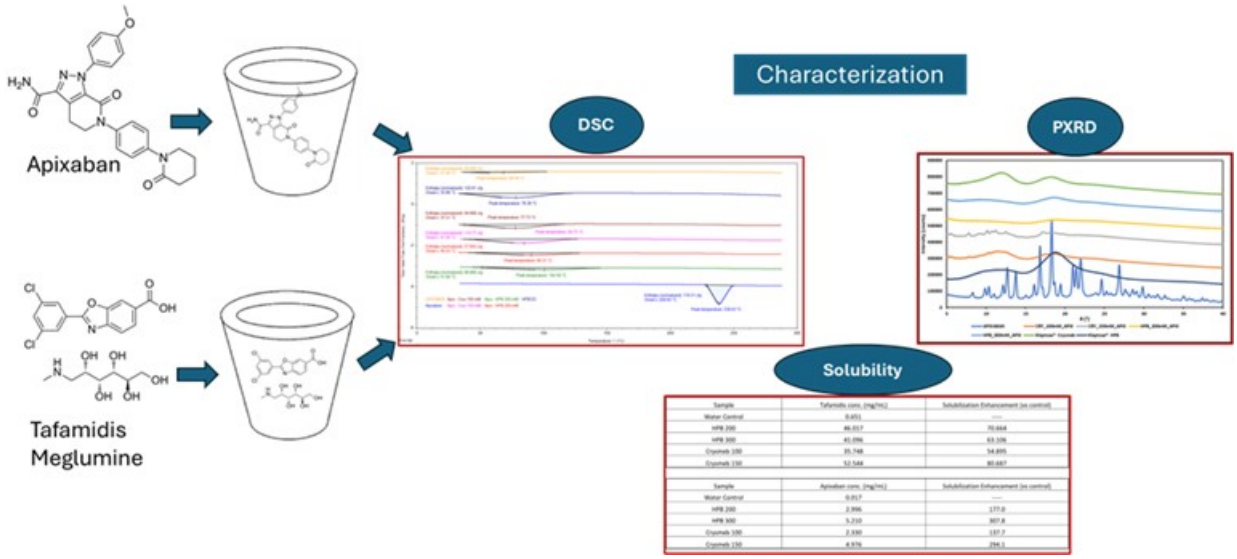

Figure 1. Apixaban and tafamidis meglumine graphical abstract of solubility and complex formation evaluation.

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PP09

Beta-cyclodextrin derivatives efficiency in solubilizing Itraconazole

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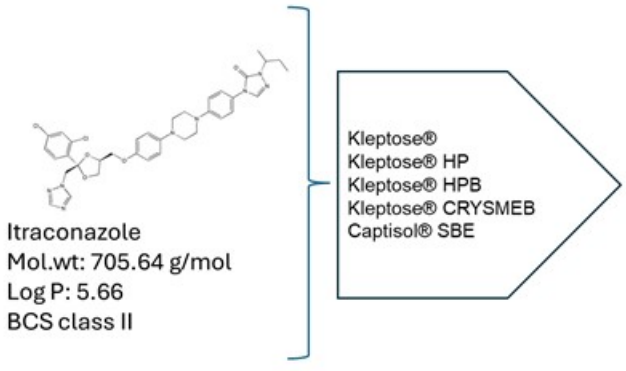
Itraconazole is a wellf-known BCS Class II API with high molecular weight (705.64 g/mol) and high log P (5.66), causing challenges in formulation due to its very low water solubility (0.238 µg/ml). The aim of this study was to screen the solubilization efficiency of different β-cyclodextrin derivatives KLEPTOSE® (β-cyclodextrin], KLEPTOSE® HP (hydroxypropylated β-cyclodextrin), KLEPTOSE® HPB (hydroxypropylated β-cyclodextrin), KLEPTOSE® CRYSMEB (methylated β-cyclodextrin), and Captisol® SBE.

Saturation solubility of itraconazole was evaluated based on the phase solubility technique developed by Higuchi and Connors. Stability constant and complexation efficiency were calculated using phase solubility diagrams. Also, to prove complex formation, filtrates were lyophilized (Freezone 2.5 Plus, Labconco®, Kansas City, MO) and evaluated by differential scanning calorimetry (DSC). Complexation efficiency ranking KLEPTOSE® Crysmeb> KLEPTOSE® HPB> KLEPTOSE® HP> KLEPTOSE® = Captisol® SBE. Even both KLEPTOSE® HP (High MS=0.85) and KLEPTOSE® HPB (Medium MS=0.65) are hydroxypropylated β-cyclodextrins, due to their different degree of substitution, they display different complexation potential with Itraconazole. KLEPTOSE® CRYSMEB is a methylated derivative of β-cyclodextrin which displays a better solubilization capacity (1561 times vs. water solubility). DSC thermogram demonstrates complexation of itraconazole with all screened cyclodextrins.



Summary of itraconazole:CD complexation

Itraconazole-CD Stability comstant ($K_{1:1}$) and Complexation efficency (CE)

Cyclodextrin	Generic name	R	Molucuar weight (g/mol)	m (slope) (ITZ)	S_0 (mM)	$K_{1:1}$ (ITZ)	CE (ITZ)
Kleptose® BCD	β-cyclodextrin	H	1135	0.00040	0.00033	1.21	0.00040
KLEPTOSE ® HPB (medium MS, approx. 0.65)	Hydroxypropyl-βcyclodextrin	CH2CHOHCH3	1400	0.00250	0.00033	7.57	0.00251
KLEPTOSE ® HP (high MS, approx. 0.85)	Hydroxypropyl-βcyclodextrin	CH2CHOHCH3	1481	0.00230	0.00033	6.96	0.00231
Kleptose® Crysmeb	2-O-methyl β-cyclodextrin	CH3	1191	0.00390	0.00033	11.83	0.00392
Captisol SBEBCD	Sulfobutyl β-cyclodextrin	(CH2)4-SO3Na	1451	0.00040	0.00033	1.21	0.00040

DSC

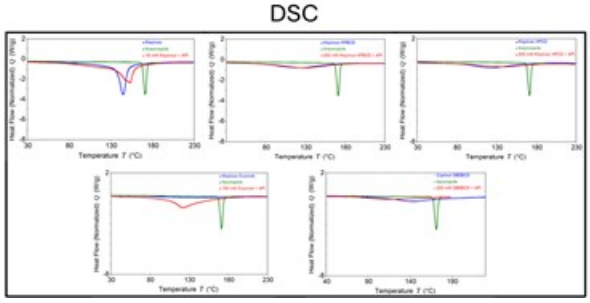


Figure 1. Itraconazole graphical abstract of solubility and complex formation characterization.

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PP10

Chromatography free synthesis of $2^A,2^B$-disulfonated β-cyclodextrin

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Cyclodextrins (CDs) derivatives are widely applied in various industries, often due to their ability to form inclusion complexes with hydrophobic guest molecules. While mono-substituted CD derivatives are well-established—with over 1400 peer-reviewed articles describing efficient, chromatography-free syntheses using arylsulfonate intermediates [1]—the synthesis of isomerically pure di-substituted CDs remains significantly more challenging. Reported methods often rely on column chromatography, limiting scalability and broader application.

We describe a practical, chromatography-free synthesis of isomerically pure $2^A,2^B$-disulfonated β-cyclodextrin using a readily prepared benzophenone-3,3′-disulfonyl imidazole derivative, adapted from the work of Teranishi (2000) [2]. All reactants and product were obtained via scalable precipitation and recrystallization steps, avoiding chromatography entirely. The $2^A,2^B$-disulfonated β-CD was isolated in up to 33% yield with >96% purity, as confirmed by 1D/2D NMR, FTIR, and HPLC-MS analyses.

This di-functionalized β-CD serves as a versatile scaffold for further derivatization into azido or amino-CDs, enabling novel applications such as the synthesis of linear CD-based polymers and nanostructured materials (e.g., electrospun nanofibers), with the possibility to explore isomerically pure di-functionalised CD for further applications also can be realised.

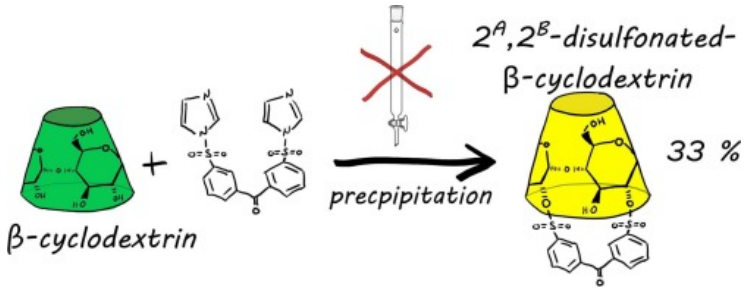

Figure 1. Producing isomerically pure $2^A,2^B$-disulfontaed β-cyclodextrin without chromatography.

Acknowledgements: supported by the Ministry of Education, Youth and Sports of the Czech Republic (grant number LUAUS23155), and by the Ministry of Education, Youth and Sports of the Czech Republic and the European Union European Structural and Investment Funds in the frames of Operational Programme Research.

[1] P. Kasal, J.Jindřich, *Molecules* (2021) 26(16), 5065.
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PP11

Pinostilbene: anticancer evaluation and cyclodextrin encapsulation to overcome physicochemical limitations of this resveratrol derivative

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Pinostilbene is a naturally occurring methoxylated stilbene with interesting health-promoting properties, including antioxidant, antimicrobial, and neuroprotective effects [1]. However, its potential anticancer activity remains largely unexplored. Like other stilbenes, pinostilbene is highly unstable, rapidly degrading under stress conditions, and has poor water solubility, limiting its applicability as a therapeutic agent. This study aims to further investigate its anticancer properties while addressing its physicochemical limitations through encapsulation in cyclodextrins—cyclic oligosaccharides known to enhance the solubility and stability of hydrophobic compounds.

A screening of different cyclodextrins was conducted to determine the one with the highest encapsulation constant and to establish the encapsulation stoichiometry, using fluorescence spectroscopy. The protective effect of cyclodextrins against degradation was assessed through spectrophotometric measurements over time. Additionally, the anticancer activity of pinostilbene was evaluated in vitro using the MTT assay in Caco-2 colorectal cancer cells.

Hydroxypropyl-β-cyclodextrin was the most effective encapsulating agent with the highest encapsulation constant (KF = 10,074.45 ± 503.72 M^{-1}) with a 1:1 stoichiometry. Encapsulation significantly improved the stability of pinostilbene, reducing its degradation from 31% to less than 15% over three months, while increasing its water solubility by 10-fold. The *in vitro* assays revealed promising antiproliferative effects in colorectal cancer cells, comparable to those of resveratrol.

Pinostilbene shows strong in vitro antiproliferative activity, highlighting its potential as a drug candidate. Moreover, its physicochemical drawbacks can be mitigated through cyclodextrin encapsulation, enhancing its solubility and stability. These findings open new possibilities for the pharmaceutical and food industries, promoting the development of pinostilbene-based formulations.

Acknowledgements: Spanish Ministry of Science and Innovation, project PID2021-122896NB-I00 (MCI/AEI/10.13039/501100011033/FEDER, UE). Predoctoral contract (for I.C.) financed by the University of Murcia (Región de Murcia, Spain). Predoctoral contract (for F.J.V.S., number FPU21/03503) financed by the Ministry of Universities (Spain). Ramón y Cajal Contract funded by MICIU/AEI/10.13039/501100011033 and by the FSE+ (for A.M, Grant RYC2023-043196-I).

[1] Koh Y-C, Lin S-J, Nagabhushanam K, Ho C-T, Pan M-H. *Mol Nutr Food Res.* (2022) 66(11), e2200146.

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PP12

Characterization of β-Cyclodextrin–PMDA Nanosponges: NanoEnviCZ Research Infrastructure

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In order to develop an efficient sorbent material for the removal of perfluorinated compounds (PFAS) [1], a reaction between β-cyclodextrin (BCD) and pyromellitic dianhydride (PMDA) was carried out. This reaction leads to the formation of ester bonds between the carboxyl groups of PMDA and the hydroxyl groups of BCD, resulting in a three-dimensional crosslinked polymer network. The final material, referred to as a nanosponge [2], is insoluble in water and exhibits a nanoporous structure with a high sorption potential for PFAS.

To confirm the formation of ester bonds, evaluate the spatial arrangement of the polymer network, detect structural changes relative to the starting compounds, and assess the thermal stability of the polymer, it was necessary to employ a range of advanced analytical techniques. The characterization was therefore performed using nuclear magnetic resonance (NMR), Fourier-transform infrared spectroscopy (FTIR), Raman spectroscopy, and thermogravimetric analysis (TGA).

Given the complexity and cost of these methods, the analyses were carried out using the instrumental facilities of the research infrastructure NanoEnviCZ. This infrastructure offers open access to state-of-the-art analytical techniques and instrumentation for the investigation of nanomaterials, including the study of their properties, stability, and impact on the environment, living organisms, and human health. NanoEnviCZ is available to researchers from both academia and industry, providing substantial support for the advancement of materials research in these areas.

Acknowledgements: The authors acknowledge the assistance provided by the Research Infrastructure NanoEnviCz, supported by the Ministry of Education, Youth and Sports of the Czech Republic under Project No. LM2023066.

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[2] I. Krabicova, et al. *Polymers* (2020) 12, 1122.

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PP13

SEAclodextrin: Bioorthogonal platform for selective *N*-term cysteinyl peptide and protein conjugation

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Cyclodextrins (CDs) have emerged as versatile platforms for drug delivery, biomolecule conjugation, and supramolecular chemistry. Traditional approaches to functionalizing CDs for peptide or protein bioconjugation relies on azide-alkyne cycloadditions, maleimide-thiol reactions, or activated esters. However, these strategies require prior chemical modifications of peptide or protein side chains to selectively and regioselectively introduce an anchor, typically through alkyne, cyclooctyne or maleimide derivatives. In this work, we report the development of novel α- and β-cyclodextrin derivatives bearing a blocked thioester bis(2-sulfanylethyl)amide) (SEA)[1] as a bioorthogonal handle for the site-selective conjugation of *N*-terminal cysteinyl peptides or native folded cysteinyl proteins. This approach relies on native chemical ligation (NCL)[2], which takes advantage of the high reactivity and specificity of thioesters toward *N*-terminal cysteines, enabling efficient conjugation under physiological conditions (pH 7, 37°C). Additionally, this strategy offers enhanced selectivity, as *N*-terminal cysteines are less prone to off-target reactions compared to internal thiols, which are commonly targeted in maleimide-based bioconjugation. Our approach also provides metal-free reaction conditions, eliminating the need for Cu^{2+} or costly DBCO linkers. Finally, this novel thioester-based strategy expands the bioconjugation toolkit for cyclodextrins, opening new possibilities for protein immobilization, targeted drug delivery, and biomaterial functionalization.

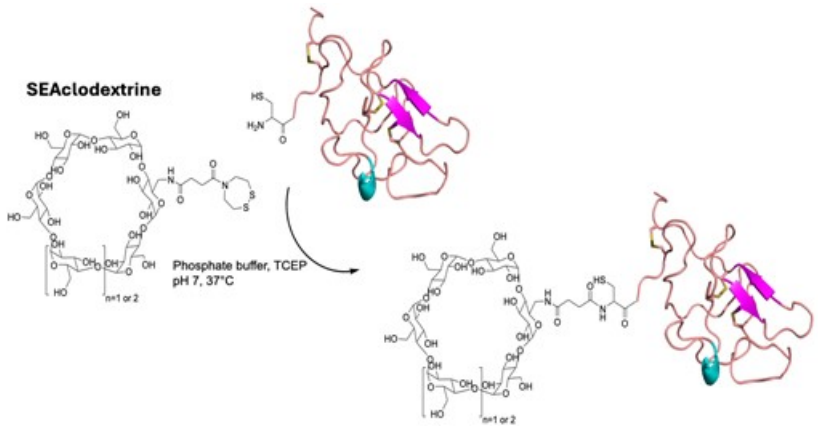

Figure 1. SEAclodextrine platform for cysteinyl protein bioconjugation.

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[2] L. Raibaut, N. Ollivier, O. Melnyk, *Chem. Soc. Rev.* 2012, 41, 7001−7015.

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PP14

Host-Guest Interaction Between β-Cyclodextrin and Dimethomorph: A Study of Complexation Behavior

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β-Cyclodextrins (β-CDs) are cyclic oligosaccharides that present a hydrophilic surface and a hydrophobic cavity and are widely used in various fields thanks to their non-toxicity properties. They can interact with many classes of hydrophobic molecules such as drugs or pollutants [1]. The aim of this work is to describe the host-guest interaction between β-CD and dimethomorph (DMM), a fungicide commonly used in agriculture. The interaction between these two molecules has been studied using molecular dynamics simulations, in order to understand the kinetic mechanism, the thermodynamic of the interaction and the geometry of the complexation. The thermodynamic analysis confirms that two stable complexes are formed with both the E and Z isomers of DMM. The cyclodextrin interacts only with the aromatic part of the two isomers but two differents behaviour are observed. For the DMMZ isomer only one type of complex is formed, whereas for DMME both the aromatic rings of the molecule interact with the cyclodextrin cavity (Figure1). This stable and reversible host guest interaction can be a good starting point for the formulation of β-CD based materials for the elimination of environmental pollutants[1].

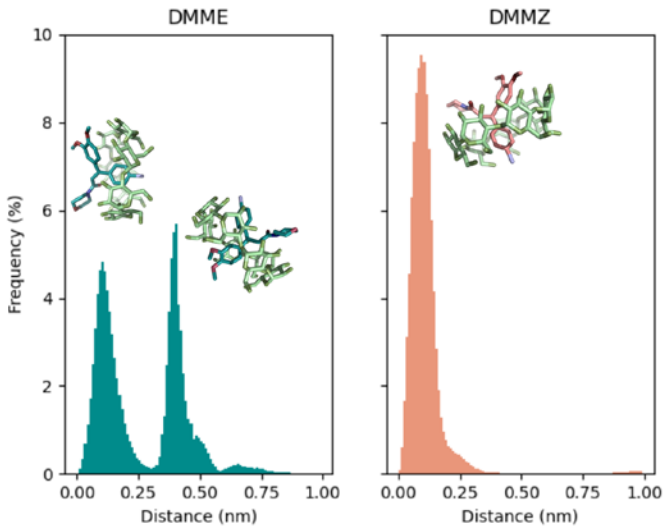

Figure 1. Illustration of host-guest interaction between DMM and β-CD.

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PP15

Macrocyclic ligands giving access to robust photosensitizers based on copper complexes

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A recent study conducted by our two teams has shown that macrocyclic ligands containing a coordinating unit of the diphosphine or diimine type can be used to stabilize $[Cu(NN)(PP)]^+$ complexes in solution and enhance their luminescent properties.[1] We now aim at developing even more efficient and robust copper(I) complexes. To modulate the photophysical properties of this new class of photosensitizers, cyclodextrin (CD)-based macrocyclic diphosphines have been combined with various functionalized diimines (bpy, phen, etc.) bearing either electron-donating or electron-withdrawing groups at various positions of the nitrogen ligand. The design of highly robust photosensitizers based on these principles should ultimately open up new perspectives in photocatalysis, as it will avoid the use of complexes based on environmentally harmful and expensive second- and third-row transition metals.[2]

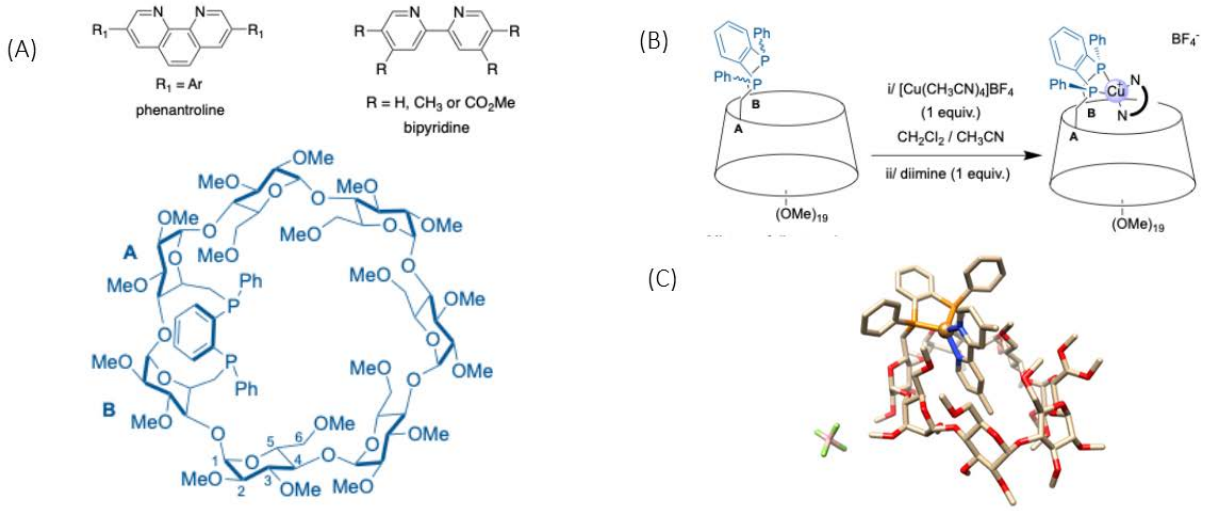

Figure 1. A) Functionalized diimine and diphosphine ligands; B) Complexation of Cu(I) by the CD-based diphosphine and a functionalized diimine ligand; C) X-Ray crystal structure of a $[Cu(NN)(PP)]^+$ complex showing the encapsulation of a 4,4'-functionalized bpy ligand.

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PP16

Impact of KLEPTOSE® CRYSMEB on Enveloped Viruses

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Cholesterol (Chol) in lipid rafts plays critical roles in many aspects of the virus life cycle. Depletion of Chol using cyclodextrin derivatives (CD) has a major impact on cell entry, replication, and survival of various enveloped viruses, including Influenza A, Parainfluenza type 3, Coronavirus, Newcastle Disease virus, etc. [1,2]. KLEPTOSE® CRYSMEB is a methylated cyclodextrin derivative that exhibits fewer methyl group substitutions compared to randomly methylated cyclodextrin (RAMEB). The aim of this study was to assess the impact of KLEPTOSE® CRYSMEB on various enveloped viruses by evaluating percentage viral inhibition using positive controls (Table 1). Hemolytic effects were assessed using human red blood cells. KLEPTOSE® CRYSMEB showed no antiviral activity against Adenovirus, Influenza, RSV, and HSV-1, but it was effective against betacoronavirus 1 and SARS-CoV-2 to a greater extent than hydroxypropyl β-cyclodextrin (HPβ-CD), with less toxicity than remdesivir (Figure 1 and 2). These results indicate that the antiviral effects of methylated cyclodextrins are species-dependent and related to the nature of the substitutions. However, the cytotoxicity of CD's must be considered, as their impact on Chol can affect both the virus envelopes and the host cell membranes. Indeed, hemolysis results showed that KLEPTOSE® CRYSMEB has a lower impact on cellular membranes than RAMEB, with a cytotoxicity level between HPβ-CD and RAMEB (Figure 3). The results demonstrated that KLEPTOSE® CRYSMEB can be used as an antiviral, particularly against coronaviruses, with less cytotoxicity than RAMEB.

Virus	Strain/serotype	Cell line	Control compound
Adenovirus	Type 5 (E500)	HeLa	Cidofovir
Influenza A	A/Panama/2007/99 (H3N2)	MDCK	Oseltamivir
RSV	Human respiratory syncytial virus (ATCC® VR-1540™)	HeLa	Ribavirin
HSV-1	SC16	Vero	Acyclovir
Coronavirus	Human coronavirus 229E ATCC® VR-740™	16HBE/MRC5	Remdesivir
Coronavirus	Betacoronavirus 1 OC-43 ATCC® VR-1558™	16HBE/H292	Remdesivir
Coronavirus	Betacoronavirus SARS-CoV-2/human/Liverpool/REMRQ0001/2020	Vero E6 TMPRSS2	Remdesivir

Table 1. Tested conditions.

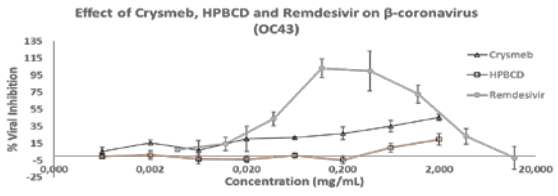

Figure 1. Effect of cyclodextrins on coronaviruses (n=3)

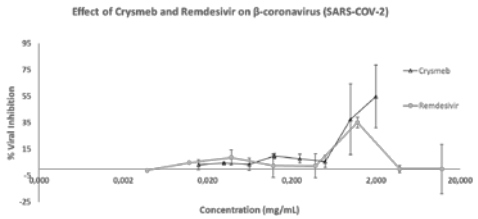

Figure 2. Effect of cyclodextrins on SARS Cov2 (n=3)

	HPβ-CD	CRYSMEB®	RAMEB
NOEC (mg/mL)*	5	2	<0.5
EC10 (mg/mL)	12.4	4.9	1.7
EC50 (mg/mL)	30.7	9.2	3
EC90 (mg/mL)	60.3	14.5	4.5
EC100 (mg/mL)	91.0	19.2	6.8

Figure 3. Haemolytic effects of CD's

Acknowledgements: Eurofins CEREP (Fr) and Charles River Laboratories, Portishead (UK)

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PP17

SuFEx-Enabled Cyclodextrin Functionalization and Connection: Click-II Chemistry Utilized for Innovative Cyclodextrin Modifications

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Click chemistry is a conceptual framework for functional molecular assembly, emphasizing a modular approach of selective reactions for the rapid synthesis of useful new compounds in search of function. Copper(I)-catalyzed azide–alkyne cycloaddition [1] (CuAAC) and sulfur(VI) fluoride exchange [2] (SuFEx) are often referred to as Click-I and Click-II, respectively, by Prof. Sharpless and co-workers. Over the past decade, SuFEx reactions have illuminated some of the unique advantages of click chemistry, including facile assembly of versatile small-molecule libraries and rapid entry to novel families of intriguing materials[2,3]. While CuAAC click chemistry is being extensively utilized in numerous emerging areas of glycoscience[4], the application of SuFEx click reactions in the field of carbohydrate and cyclodextrin (CD) chemistry has so far remained underexplored[5,6]. Here we present for the first time innovative CD modifications enabled by SuFEx click chemistry. After equipped with appropriate SuFEx hubs, the resulting CD–SuFEx intermediates can click with a broad spectrum of commonplace building blocks, thus handily introducing a wide range of desired functionalities and drastically increasing accessible chemical space.

Acknowledgements: We are grateful to Prof. Dr. K. Barry Sharpless (Scripps Research) for his valuable advice. We thank Dr. Brad Herberich and Dr. Eric Kuenstner (Beren Therapeutics) for helpful discussions.

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PP18

Readily Accessible Host Library and Screening Approach for High Binding Affinity Host-Guest Complex Formation: Case Study for Cyclodextrin-Bilirubin Complex

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Cyclodextrin sequestration is a proven, highly translatable therapeutic modality. We report a streamlined approach to rapidly identify high-affinity, selective cyclodextrin-based sequestration agents demonstrated through a case study targeting bilirubin. Cyclodextrins are versatile scaffolds for ligand sequestration, but their challenging modification has limited broader applications in drug delivery and toxin removal. Here, we generated a readily synthesizable library of approximately 100,000 β- and γ-cyclodextrin derivatives by modifying monomeric units using diverse, scalable reactions. This extensive library was initially screened in silico to eliminate low scoring compounds, followed by molecular dynamics simulations to refine hit selection. Our workflow yielded 12 promising candidates, eight of which were selected and synthesized. Binding interactions were confirmed through circular dichroism, UV, and NMR spectroscopy. Based on experimentally determined binding affinity, our top compound showed about 10-fold improvement compared to native cyclodextrin. Notably, NMR revealed a unique binding mode where bilirubin engages the cyclodextrin host with one portion inside the hydrophobic cavity and the other interacting with the polar exterior. This suggests further binding affinity enhancement through targeted modifications near the bilirubin binding region of the cyclodextrin host is possible. Preliminary *in vivo* results show vascular bilirubin retention in rats and reinforce the translational potential of cyclodextrin-based therapeutics and our screening platform. Overall, our integrated computational and experimental strategy offers a promising pathway for developing cyclodextrin derivatives for therapeutic applications.

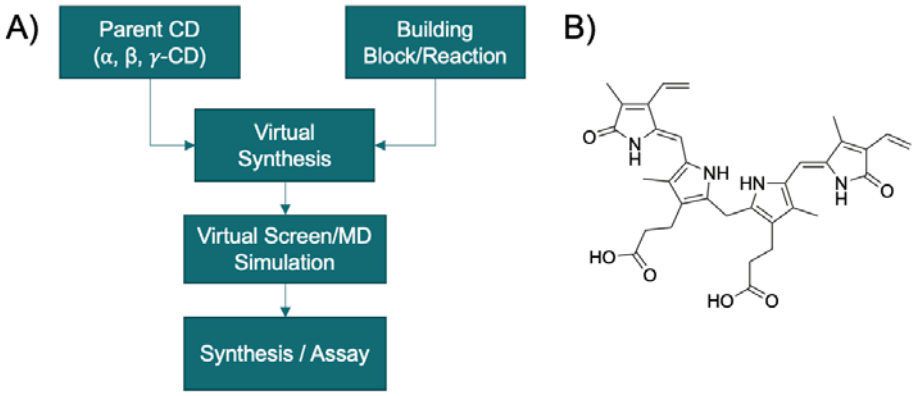

Figure 1. A) Schematics of virtual library preparation and screening cascade. B) Bilirubin structure

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3D Printed Scaffolds Decorated with Cyclodextrins for Signal Trapping

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Quorum sensing (QS) is a communication mechanism that enables bacteria to coordinate different processes at the population level. The mechanism is based on the release of molecules, autoinducers, which allow bacteria to regulate gene expression when they reach a critical population density or “quorum”. It has been demonstrated that some bacteria, e.g. *Pseudomonas aeruginosa* and *Staphylococcus aureus*, use QS to control processes such as virulence, toxin release and biofilm formation [1]. In terms of wound treatment, biofilm formation significantly contributes to implant and to tissue regeneration scaffolds failure, hindering tissue regeneration and chronification of the wound [2]. The role of QS communication and the increment of antibiotic resistance point out the necessity of antibiotics alternatives or new approaches to treat infections.

In this work we propose an approach to prevent biofilm formation on 3D printed medical devices by covalently bonding cyclodextrins to the polymer network. The potential of cyclodextrins to capture QS signaling molecules has been previously reported [1]. However, the use of cyclodextrin as a part of the polymer matrix in 3D printing (3DP) has been barely explored. Based on this, we synthesized vinyl and acrylic cyclodextrin derivatives that can act as monomers in digital light processing (DLP) printing, a subclass of vat photopolymerization technology. DLP printing allows the fabrication of hydrogel devices which can act as scaffolds for soft tissue regeneration. Thus, we hypothesize that the attached cyclodextrins will act as molecular trappers of autoinducers and therefore, inhibiting bacterial communication. Initial attempts to incorporate cyclodextrins into the polymer network resulted in poor inclusion complexes formation, probably due to the high crosslinking density of the polymer network that can occlude the cyclodextrin cavity. To overcome this, we synthesized mono- and low-substituted cyclodextrin on the 6-OH with a spacer of 8 to 12 atoms distance from the cavity to reduce steric hindrance. Direct printing and post-functionalization on the surface were explored to attach cyclodextrin on the network.

Acknowledgements: The work was supported by MCIN/AEI/10.13039/501100011033 [PID 2020-113881RB-I00], Spain, Xunta de Galicia [ED431C 2020/17], FEDER, and- Next-Generation EU-(NRRP)-M4-C2-I1.1, PRIN 2022 PNRR D.D. 1409 14-09-2022-3D-VOCE (P2022JWF3P). ASR acknowledges a PRE2021-098268 fellowship financed by MCIN/AEI/ 10.13039/501100011033 and FSE+.

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PP20

Collapse of liposomes revealed by binding of palmitate and oleate ions with cyclodextrins

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Detailed knowledge on lipid-cyclodextrin (CD) interaction is crucial for precise modeling of (non)equilibrium processes in complex biologically, pharmaceutically and dermatologically relevant matrices [1]. Depending on CD type its presence next to (phospho)lipid liposomes provide vast responses: starting by lipid extraction, through liposome disruption, up to formation of solid precipitate [1-4].

In present work, the interaction of two long alkyl-chain fatty acid anions palmitate and oleate with native β-, γ- and modified 2-hydroxypropylated and methylated α- and β-CDs in water was examined using the isothermal titration calorimetry (ITC) [5,6]. The obtained heat data at several temperatures were treated simultaneously (if possible) allowing the estimation of a thermodynamically consistent temperature dependence of the equilibrium constant as well as the enthalpy for the sequential formation of the inclusion complexes of varied stoichiometries. Thermodynamic quantities for complexation are discussed in terms of their temperature dependence and structural features as cyclodextrin cavity size and modification [5-7]. Using present data the binding mode of CDs to diacylphospholipids and triacylglycerides bearing identical alkyl moieties is revealed.

Acknowledgements: Financial support of this work from Institutional funding of the University of Chemistry and Technology Prague, is gratefully acknowledged.

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PP21

Impact of Methylated cyclodextrin KLEPTOSE® CRYSMEB on cell proliferation in cancer context

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Cell proliferation is a major factor in the development of cancers. In other words, the process by which cells multiply uncontrollably plays a crucial role in the formation and progression of cancerous tumors. Consequently, the primary goal of anticancer treatments is to reduce the number of cancer cells present in the body. To achieve this, one possible strategy is to use an agent that eliminates cancer cells combined with an excipient that inhibits cell proliferation. In this context, cyclodextrin derivatives are interesting because offers low toxicity and seem capable of inhibiting cell proliferation, linked to the remove of cholesterol by cyclodextrins [1]. Our KLEPTOSE® CRYSMEB is a methylated cyclodextrin derivative that exhibits fewer methyl group substitutions compared to randomly methylated cyclodextrin (RAMEB)

The aim of this study was to investigate the effect of KLEPTOSE® CRYSMEB on the proliferation of cancer cells. To this end, we used different cancer cell lines from various organs (breast, kidney, and lung) as well as a healthy cell line derived from extracellular matrix. After cytotoxicity tests, we monitored cell proliferation, compared to aphidicolin, known to inhibits cell cycle progression. First, through counting, we observed that cell growth was reduced in the presence of KLEPTOSE® CRYSMEB, only in cancer cells (Figure 1). This observation was confirmed by a decrease in the number of cells in the S phase through cytometry. An evaluation by flow cytometry also allowed us to confirm that KLEPTOSE® CRYSMEB had a cytostatic effect rather than a cytotoxic one. These experiments highlight the antiproliferative effect of our methylated cyclodextrin, which is used as a pharmaceutical excipient.

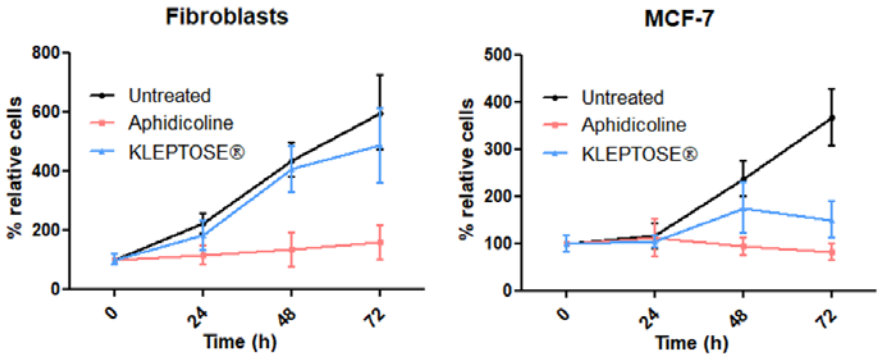

Figure 1. Reduction of cancer cell growth using KLEPTOSE® CRYSMEB.

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PP22

Influence of CDs on loratadine stability: accelerated and photostability studies

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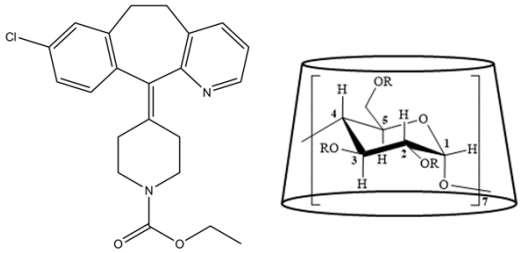
Loratadine (LOR) is a second-generation antihistaminic, characterized by its low solubility and high permeability. Cyclodextrins (CDs) are cyclic oligosaccharides that are often used to enhance the solubility of drugs by formation of the inclusion complexes. However, this may affect their physico-chemical properties, such as stability [1].

In this work, LOR stability was studied in the presence of β-CD and its derivatives, hydroxypropyl (HP-β-CD), randomly methylated (RM-β-CD) and sulfobuthylether sodium salt (SBE-β-CD). Loratadine and binary systems with CDs were prepared by grinding in the stoichiometric ratio 1:1 and/or 1:2. Accelerated stability studies were performed according to ICH guidance by weighing samples and placing them in stability chambers at 40 °C and 75% relative humidity for six months. Samples were collected after 0, 1, 2, 3, 4, 5, and 6 months. Photostability study was performed by exposing weighed samples for 141.2 h to daylight source (8.5 Klux) and 40h to a UV source (5 W m^{-2}) to ensure that standard ICH Q1B photostability testing conditions were achieved [2]. All samples were analysed by ultrahigh-performance liquid chromatography.



β-CD	R = –H
HP-β-CD	R = –H or –$CH_2CH(OH)CH_3$; DS = 4.5
RM-β-CD	R = –H or –CH_3; DS = 12
SBE-β-CD	R = –H or –$(CH_2)_4SO_3Na$; DS = 6.5

Figure 1. Structures of loratadine and β-cyclodextrin and its derivatives.

Acknowledgements: This work was supported by the Croatian Science Foundation under the project number HRZZ-IP-2022-10-6033.

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PP23

Solid state characterization of Cinnarizine: β-cyclodextrin complexes prepared by grinding

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Among the different techniques proposed for preparing cyclodextrin inclusion complexes in the solid state, mechanochemical activation by grinding appears as a fast, highly efficient, convenient, versatile, sustainable, and eco-friendly solvent-free method. [1] Previously we reported the preparation of Nabumetone (NAB) binary mixtures with various β-cyclodextrins (β-CD) in solid state by mechanochemical activation in high energy vibrational mills. Processing NAB with CDs yielded powdered products, where the level of drug amorphization depended on the used β-CD derivative and applied grinding conditions. [2]

In this study, we applied mechanochemical activation by grinding to prepare solid β-CD complexes of Cinnarizine (CIN), a poorly soluble antihistamine drug. The grinding process in high-energy ZrO_2 vibrational mills was monitored by calculating the relative degree of CIN crystallinity based on the results of differential scanning calorimetry analyses. Experimental conditions such as the size of grinding balls, total grinding time and frequency were varied to achieve complete drug amorphization and probable formation of inclusion complex in solid state. The final products obtained by grinding were additionally characterized by powder X-ray diffraction and FT-IR spectroscopy.

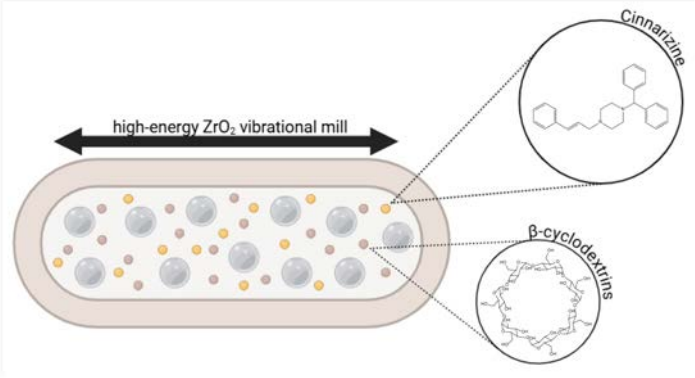

Figure 1. Schematic representation of CIN:β-CD mixture grinding process.

Acknowledgements: This work was supported by the Croatian Science Foundation under the project number HRZZ-IP-2022-10-6033.

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PP24

New type of single-isomer cyclodextrins for chiral separation of APIs with gas chromatography

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Asymmetric cyclodextrins differently persubstituted on both secondary OH-groups were developed in collaboration with MEGA S.r.l. (Italy) for chiral gas chromatography. This new family of CDs are characterised by further increase of the already existing asymmetry of the CDs. This increased asymmetry is expected to allow enhanced separation of enantiomers, which in turn results in better analytical capabilities, especially in the case of hard to separate isomers. [1]

This study focuses on the chiral separation of APIs with gas chromatography using the columns loaded with the new type of single-isomer cyclodextrins and comparing them to the already existing commercially available columns.

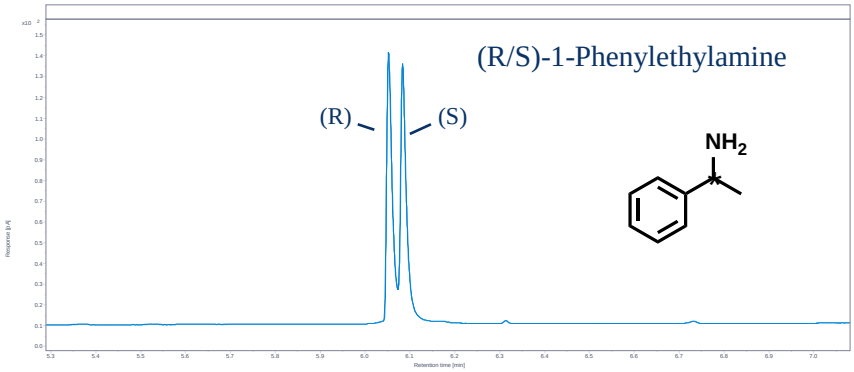

Figure 1. Example of chiral separation of enantiomers with GC using heptakis(3-O-acetyl-2-O-methyl-6-O-tert-butyl-dimethyl-silyl)-BCD bonded column

Acknowledgements: Thanks are due to Stefano Galli from MEGA S.r.l. for creating and providing the new columns for CycloLab.

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PP25

Preparation of novel alkylthio-cyclodextrin derivatives against quorum sensing

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Bacterial communication, called Quorum Sensing (QS) is a cell density dependent signaling process that allows the microbial population to behave as a multicellular organism in colonizing the host, forming biofilms, producing virulence factors, and thus adapting to changing environments. This communication system is based on the production and detection of extracellular signal molecules (called autoinducers), e.g. acyl-homoserine lactone type signals, AHLs). The inhibition of QS, Quorum Quenching (QQ) involves several different molecules and methods, which have in common, that they do not kill or exert selective pressure on the bacteria, but only prevent communication between cells. Direct modulation of this microbial communication is a new wave strategy; a potential tool for inhibiting QS is trapping the signal molecules.[1]
Nowadays, cyclodextrins (CDs) are widely used due to their ring structure and their ability to form inclusion complexes. According to previous studies, they can reversibly encapsulate the AHL molecules in Gram-negative bacteria, preventing them from binding to the receptors and interrupting the communication.[2]

The aim of the research was to develop a series of water-soluble mono-alkylthio-CD derivatives randomly substituted with sulfobutyl (SB), hydroxypropyl (HP), quaternary amino (QA) functional groups) with high complexation rate to signal molecules and a novel synthetic approach. These derivatives were characterized using NMR techniques, HPLC-MS and CE. Furthermore, short-term microbiological tests were performed in different bacterial model systems to investigate the potential QS-disrupting ability of the newly prepared cyclodextrin derivatives and to assess their bioactive potential by monitoring the effect on QS-mediated processes and viability using different endpoints.

The results showed that the contact time, the concentration, and the structure of the cyclodextrins had a significant influence on both the viability of the cells and on the processes regulated by the bacterial communication.

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α- cyclodextrin microsponges as a tool for the topical delivery of *Pistacia terebinthus* extract

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Plants' species from the genus *Pistacia* L. (Anacardiaceae) have been traditionally used to treat skin conditions and showed great potential for skin antioxidant and anti-aging applications [1]. The encapsulation of *Pistacia terebinthus* extract in α-cyclodextrin microsponges (α-CD-MS) is investigated as a strategy to develop a topical formulation, facilitating extract dissolution, preventing its thermal and light-induced degradation and providing prolonged release.

A serum based on Cró thermal water, from Beira Interior of Portugal, and containing extract-loaded α-CD-MS was formulated. The use of Cró thermal water may enhance the efficacy of *P. terebinthus* extract, since it has demonstrated numerous therapeutic benefits due to its mineral composition [2]. MS based on α-cyclodextrin and carbonyldiimidazole as crosslinker were synthetized, suspended in thermal water and loaded by incubation with *P. terebinthus* extract. Hydroxyethyl cellulose (2% w/v) was then added as rheological modifier to obtain the suitable formulation viscosity. The α-CD-MS were characterized determining the physico-chemical parameters, amount of extract loaded (loading capacity and encapsulation efficiency), *in vitro* release kinetics. The quantitative analysis of *P. terebinthus* extract was performed using gallic acid as a marker by spectrophotometer analysis. The Cró thermal water-based serum formulation were evaluated in comparison with serum prepared with distilled water, analyzing rheological properties, occlusion potential, *in vitro* release and permeation studies on porcine skin, using vertical Franz diffusion cells, and *in vitro* antioxidant activity. α-CD-MS showed the capability to encapsulate the extract and release it with controlled release kinetics.

The serum containing the extract-loaded α-CD-MS showed appropriate viscosity for topical application and low occlusivity factor. The antioxidant activity of the extract seemed to be enhanced by the presence of Cró thermal water in the serum formulation.

Based on the results, the encapsulation in α-cyclodextrin microsponges appears as a promising approach to deliver natural plant extracts in topical formulations.

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PP27

Controlled release of cyclophosphamide from a superparamagnetic β-cyclodextrin nanosponge by applying an alternating magnetic field

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This work reports the preparation of a β-cyclodextrin (β-CD) nanosponge (NS) inclusion complex with the antitumor drug cyclophosphamide (CYC), thus obtaining the NSs-CYC system. Subsequently, NSs-CYC was associated with magnetite nanoparticles (MNPs) to develop the MNPs-NSs-CYC ternary system. The formulations were characterized to confirm the deposition of MNPs on the organic matrix and the preservation of their superparamagnetic nature after association. The superparamagnetic properties of the ternary system allowed the release of CYC by magnetic hyperthermia after exposure to an alternating magnetic field (AMF). Drug release experiments were carried out at different frequencies and magnetic field intensities, complying with the Atkinson-Brezovich criterion. AMF assays demonstrated the feasibility of drug release by controlling hyperthermia. CYC release was temperature-dependent, facilitated by local heat generation via magnetic hyperthermia. Tertiary systems outperformed MNP-free formulations in terms of the amount of drug released. MTS assays demonstrated that the inclusion of CYC in the cavities of the magnetic NSs reduced the effects on mitochondrial activity compared to those observed with the free drug. Finally, magnetic hyperthermia assays showed that the tertiary system allows the generation of apoptosis in HeLa cells, demonstrating that the integrated MNPs maintain their hyperthermia-generating properties. These results suggest that the use of MNP-associated NSs could be a tool for controlled drug delivery in tumor therapy.

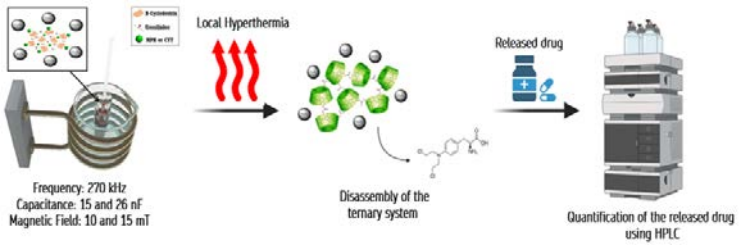

Figure 1. Schematic representation of the experiment design for the release of the guest molecule. All samples will be prepared on a dialysis tube and placed in the centre of coil.

Acknowledgements: FONDECYT Project 1251002 and FONDECYT Postdoctoral Project 3240172

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Cyclodextrin-Based Chemosensors for VOC Detection

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Monitoring indoor air quality is essential for protecting human health, given that people spend more than 80% of their time indoors. Among the various air pollutants, volatile organic compounds (VOCs) are of particular concern due to their continuous release from sources such as building materials and personal care products. Owing to their low boiling points, VOCs are primarily inhaled, which can increase the risk of allergic reactions and chronic diseases, including cancer [1]. Chemosensors offer a simple, sensitive approach for detecting these compounds [2]. In this study, we investigate the use of cyclodextrin-based conjugates for VOC detection. Specifically, we synthesized derivatives of β-cyclodextrin functionalized at the 6-position (βCD6MR) and 3-position (βCD3MR), as well as a γ-cyclodextrin derivative functionalized at the 3-position (γCD3MR), using methyl red (MR) as the reporter unit for amine detection. In these systems, MR engages in intramolecular interactions with the cyclodextrin cavity, leading to a marked reduction in pKa compared to unmodified MR—by several orders of magnitude. Circular dichroism (CD) and UV-Vis spectroscopy revealed a strong pH dependence. Titrations with VOCs such as aniline and ethylenediamine under neutral conditions produced modest spectral changes. However, under acidic conditions, increasing concentrations of these analytes induced pronounced spectroscopic shifts accompanied by a visible colour change from pink to yellow. These systems serve as model platforms for the development of highly sensitive cyclodextrin-based sensors. Moreover, their integration into 3D-printed architectures could pave the way for the fabrication of advanced, portable devices for real-time VOC monitoring.

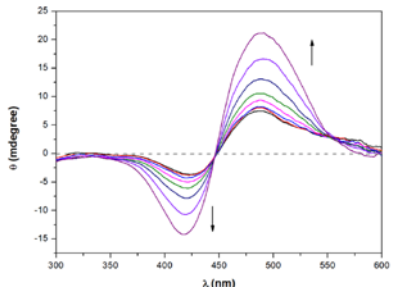

Figure 1. CD spectra of γCD3MR alone and with increasing concentration of aniline.

Acknowledgements: This research received funding from the European Union - Next-GenerationEU-National Recovery and Resilience Plan (NRRP)- Mission 4, Component 2, Investment N. 1.1, PRIN 2022 PNRR D.D. 1409 14-09-2022 - Project 3D-VOCE (P2022JWF3P), CUP E53D23016040001.

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PP29

A carboxyethyl-β-cyclodextrin polymer and a defensin derived peptide complex with wound healing potential

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Nowadays, wound management represents a major medical issue for patients with chronic and autoimmune disease due to several complications associated with pro-inflammatory milieu and bacterial accumulation [1]. Recent advances for effective wound healing consist in the fabrication of biomaterials-based dressing [2] and the therapeutic effectiveness of small peptides is being strongly emerging [3]. In this work a water soluble 6-deoxy-6-(2-carboxyethyl)thio-β-cyclodextrin polymer crosslinked with epichlorohydrin (SuBCDPS) was synthesized to include the N-terminal fragment derived from the defensin peptide. The peptide fragment was conjugated through a PEG_4 bridging moiety to an adamantane scaffold (Ada-PEG_4-Def) and characterized by FT-IR, CD, NMR and HPLC-mass analyses. The product showed negligible cytotoxicity up to 24 h and at 100 μM and promising scratch repair capabilities at 50 μM on human primary fibroblasts. Based upon the safety profile of SuBCDPS up to 100 μM, the SuBCDPS/Ada-PEG_4-Def complex was prepared and characterized by UV/Vis spectroscopy and DLS analysis (mean hydrodynamic diameter and ζ-potential). This study is propaedeutic if future fabrication of improved medical devices for wound healing applications integrating the supramolecular adduct, are considered.

Acknowledgements: This work was supported by the MUR-PNRR through the NextGenerationEU program with the project SAMOTHRACE "SiciliAn MicrOnanoTecH Research And innovation CEnter".

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PP30

Development of novel SPE packings for wastewater monitoring via electrostatic immobilization of cationic cyclodextrins

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Water pollution is a major challenge in environmental sustainability, particularly due to organic micropollutants such as pharmaceuticals and hormones that are not effectively removed by conventional wastewater treatment. These compounds can persist in the environment and even reach drinking water. To detect them, researchers analyze water samples worldwide, often applying solid phase extraction (SPE) to concentrate the analytes. CDs, known for their strong complexation ability, have already shown promise in removing such pollutants from aqueous solutions [1].

The aim of our research is to synthesize positively charged CD derivatives, which can be immobilized on various solid phases (*e.g.* silica gel, cation exchange resin) via electrostatic interaction for the development of new SPE packings. *Petr et al.* have already proved the suitability of this method by anchoring several BCD derivatives on an anionic membrane for the separation of tryptophan enantiomers [2]. During our research work, a set of known and novel BCD derivatives were prepared containing permanent positive charges. Their immobilization was performed on sulfonylpropyl-modified silica gel. Our results demonstrate the applicability of this kind of SPE packings for wastewater analysis, however, the type of solid support and the structure of the CDs need to be optimized. Our future goal is the preparation of reusable SPE cartridges that are more efficient and selective than the reversed phase cartridges available on the market.

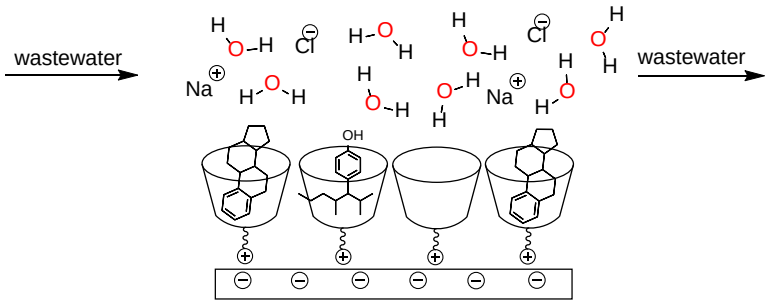

Figure 1. Bounding of organic micropollutants to cyclodextrin-based SPEs

Acknowledgements: Project No. 2024-2.1.2-EKÖP-KDP-2024-00005 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the EKÖP_KDP-24-1-BME-14 funding scheme.

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PP31

Inclusion complexes between α-Cyclodextrins and Xenon: Molecular Dynamics Simulations and Experimental study

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Xenon (Xe) is an inert noble gas that is receiving increasing attention in medical research due to its anesthetic properties, its ability to regulate metabolic processes, and its broad organoprotective effects [1]. Due to its low molecular weight and small size, xenon can be encapsulated in α-cyclodextrins (α-CDs), which possess the smallest internal cavity (0.47 – 0.53 nm) among CDs [2,3]. In this study, we present theoretical study based on molecular mechanics (MM) and molecular dynamics (MD) simulations at the atomistic level of the intermolecular interactions between α-CD and xenon. Inclusion complexes at different stoichiometries are studied, involving both encapsulation in the small cavity of the α-CD and favourable intermolecular interactions with the external surface of α-CD. In particular, by increasing the xenon concentration [4], there is a tendency for this noble gas to form aggregates of three or more atoms near the secondary and primary edges of the α-CD and on the external surface of the α-CD (see Figure 1).

Following the computational investigation, experimental work was conducted to synthesize and characterize the α-CD/Xe inclusion complex using a liquid-phase encapsulation method. The complex was prepared at three different pressures: 2, 4, and 8 bar at a constant temperature of 25 ± 1 °C. Thermogravimetric analysis (TGA) revealed a weight loss between 100 and 180 °C at 4 and 8 bar, consistent with encapsulated xenon release (Figure 2). The effective encapsulation of xenon was unambiguously confirmed by solid-phase microextraction coupled with gas chromatography–mass spectrometry (SPME-GC-MS), which detected the characteristic m/z signals of xenon and allowed monitoring of its release over time upon contact with aqueous solution.

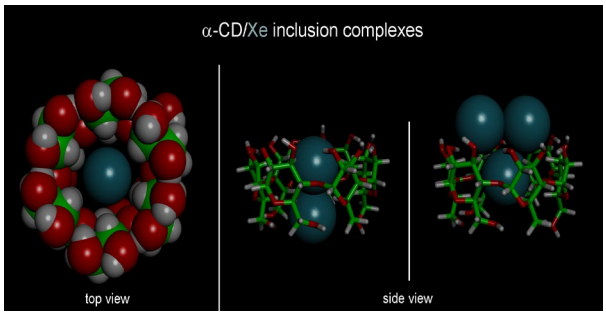

Figure 1. Optimized geometries of inclusion complexes α-CD/Xe in 1:1, 1:2, 1:3 stoichiometries

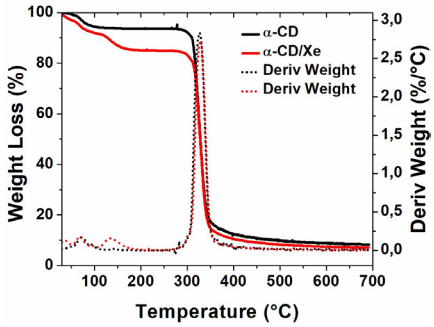

Figure 2. TGA and DTGA of α-CD and α-CD/Xe

Acknowledgements: The authors thank the CH4.0 Project for its support as part of the MUR programme 'Departments of Excellence 2023-2027' (CUP: D13C22003520001).

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PP32

Comparison of batch and flow processes for the synthesis of folic acid modified CD-derivatives

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Cyclodextrin-based drug delivery systems are extensively investigated for targeted anticancer therapy. Sulfobutylether-β-cyclodextrin (SBECD) is a polyanionic derivative with favorable pharmacological properties. However, its targeted derivatives remained underexplored, particularly those functionalized with small-molecule ligands such like folic acid.

The objective of our work was to synthesis folic acid-modified SBECD derivatives via a six-step synthetic route, starting with 6-mono-tosyl-BCD. Folic acid was selected as a crucial subunit due to its strong affinity to folate receptors that are overexpressed in various tumor cells. The linker connects folic acid to the primary side of the CD, offers steric advantages to the molecule, and facilitates the diversity of the compound library.

The synthetic route starts with the preparation of 6-mono-amino-BCD followed by linker coupling, sulfobutylation, deprotection of linker, and conjugation with folic acid. The random substitution pattern of SBECD posed considerable analytical challenges for the purification and characterization of the products. The elimination of protecting groups and isolation of the desired regioisomers required careful optimization of reaction conditions and purification methods.

To address the issues associated with conventional batch synthesis, such as prolonged reaction times and scalability concerns, we switched certain steps to flow chemistry. Firstly, the steps of linker formation and coupling with folic acid were selected for flow chemistry experiments. This approach enabled better control, faster reactions, and safer handling of intermediates, surpassing batch processes in yield and duration. The reaction with folic acid, implemented in a flow reactor, showed fewer impurities and a shorter residence time.

Our future plans include detailed physicochemical characterization of the obtained conjugates, investigation of their host-guest interactions with kinase inhibitors, and biological tests.

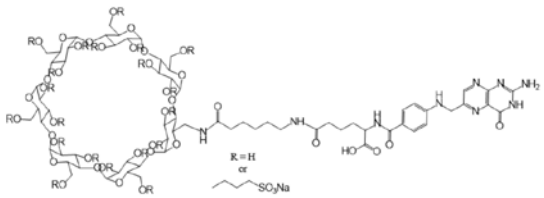

Figure 1. Folic acid conjugated SBECD

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PP33

Cyclodextrins covered gold nanoparticles as delivery systems for fluorouracil/heme oxygenase 1 (5-FU/HO-1) inhibitor hybrids

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Cyclodextrins (CDs) are versatile complexing agents which find applications in several fields. In biomedical applications, they offer unique advantages because they provide improved drug solubility and biocompatibility. In combination with metal nanoparticles (NPs), CDs form functional nanoplatforms for drug delivery, catalysis, detection and bioimaging. For cancer treatment, CDs-AuNPs nanoassemblies show a good photothermal conversion efficiency together with a drug encapsulation ability [1]. In this framework, 5-fluorouracil (5-FU) is often used as drug to treat a broad set of tumors, showing several limitations as low chemical stability, poor bioavailability and drug resistance. An effective strategy for improving 5-FU based anticancer therapies, based on the use of molecular hybrids composed of heme oxygenase 1 (HO-1) inhibitors linked to 5-FU, has been already reported [2]. In order to exploit a possible combinatorial effect between the molecular hybrids, CDs and NPs, here we proposed a first example of hydrid nanoassembly composed of Au NPs covered by CDs for the encapsulation of (5-FU/HO-1) molecular hydrids.
The nanoassembly has been prepared by means of supramolecular interactions and characterized through UV-vis absorption, F-TIR, DLS and ζ-potential measurements.
A controlled drug delivery, higher circulation time and selectivity, together with a theranostic effect due to nanoparticles properties, could be gained by our strategy.

Acknowledgements: This work has been funded by European Union- NextGenerationEU, through PRIN 2022 PNRR project (HO-Hybrid[2], Prot. P2022F4PTE, CUP B53D23025690001).

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PP34

Title To design and evaluate amphiphilic cyclodextrin derivatives as anti-aggregants for neurodegenerative diseases.

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β-Cyclodextrin (β-CD) derivatives are a promising structure for the vectorization and development of therapeutics for neurodegenerative diseases, such as Alzheimer's disease (AD), due to their biocompatibility, ability to enhance the solubility of hydrophobic molecules, and potential to penetrate the blood-brain barrier (BBB).The objective of this project is to engineer a conjugate comprising a mono-6-amino-per-methylated β-CD and a KLVFF mimetic peptide. The conjugate is designed to inhibit the aggregation of amyloid-β 42 (Aβ42), a peptide associated with amyloid plaque formation in Alzheimer's disease (AD), while concurrently enhancing its solubility and penetration into the brain. In this study, the KLVFF-mimicking peptides will be synthesized from the original sequence and improved variants, then combined with modified β-CD. Consequently, a series of conjugates will be obtained and evaluated in terms of their ability to inhibit Aβ42 aggregation. This work is currently in progress. The KLVFF-β-CD conjugates and their mimetic versions will undergo analysis to identify those most effective in preventing aggregation and neutralizing toxicity linked to soluble forms of Aβ. The present project has the potential to contribute to the development of new therapeutic approaches targeting the preliminary stages of Alzheimer's disease (AD).

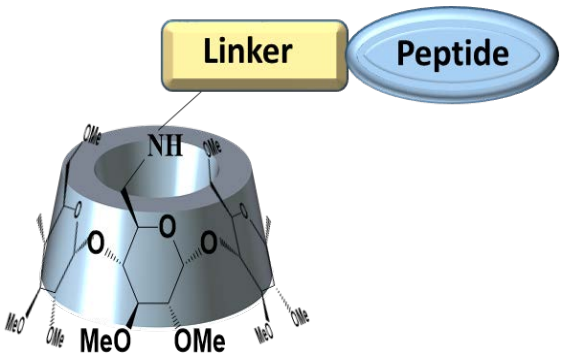

Figure 1. This is a model of target molecules against Amyloid Aβ42 aggregation

Acknowledgements: This work is supported by the PHC Tassili project [24MDU101]. The authors express their gratitude to the Laboratory of LG2A, University of Picardie Jules Verne, for technical support.

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PP35

Actuators via Host-guest Complexes for Photoswitchable Adhesives: Selective Peeling-off Property and Solvent-free Reusability

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To recycle the adhered substrates, adhesives are hoped to be peeled off from the substrates without residue under typical stimuli. Previously, our groups have reported several supramolecular adhesion systems [1]. Herein, a new photoswitchable adhesive system using actuators via stilbene-based reversible crosslinks (H-StiG-[BMA(90)-MEA]) was designed. The adhesives can be peeled off from the UV-irritated substrate without residue and can be reused without solvent dissolution.

H-StiG-[BMA(90)-MEA] was prepared through bulk copolymerization of butyl methacrylate (BMA), 2-methoxyethyl acrylate (MEA), *N*-(4-styrylphenyl)acrylamide (StiAAm), and TAcβCDAAmMe (Fig. 1a). StiAAm and TAcβCDAAmMe were dissolved in the solution of BMA and MEA and sonicated. Thermal radical initiator was then applied to the mixture and heated to form prepolymer. The prepolymer was then applied to the prepared mold and heated for 12 h at 65 °C to form H-StiG-[BMA(90)-MEA].

Selective peeling-off properties of H-StiG-[BMA(90)-MEA]: Two H-StiG-[BMA(90)-MEA] samples were attached between two plasma treated PET substrates and fixed with clips respectively. The adhesives were then heated for 30 min at 80 °C. One underwent the peeling off test immediately, and the other underwent the peeling off test after irradiated by UV light for 5 min. The initial one showed the adhesion failure, and the adhesives left on random substrates, while the UV irritated one showed the adhesion failure from the irradiated substrates with the decreasing of peel strength (Fig. 1b). Therefore, selective peeling-off adhesives without residue were achieved.

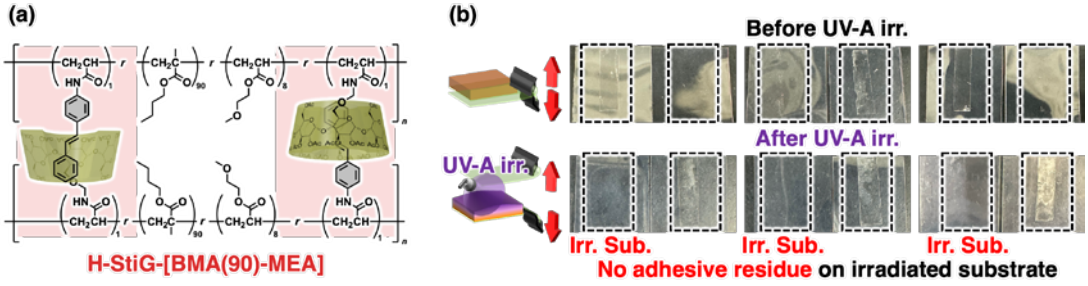

Figure 1. (a) Chemical structures of H-StiG-[BMA(90)-MEA]. (b) Failure types of the peeling-offed H-StiG-[BMA(90)-MEA] before and after UV-A irradiation.

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PP36

Passive sampling of polyol marine toxins in seawater with hyper-crosslinked cyclodextrins

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Cyclodextrin polymers have proven as efficient capture materials for marine toxins in different environments. Here we present the interaction of hexamethylene diisocyanate-based CD polymers with palytoxin-like compounds. These are potent emerging toxins responsible for human respiratory poisonings following inhalation of contaminated marine aerosols. Periodic massive proliferations of the ovatoxin-producing organism, *Ostreopsis cf. ovata*, particularly in the Mediterranean Sea, have caused severe toxic outbreaks, drawing the attention of health authorities. We carried out spiking experiments using different concentrations of palytoxin or ovatoxins and LC-HRMS detection to evaluate the suitability of CD polymers in capturing palytoxin-like compounds. Among the tested polymers, the γ-CD polymer provided toxin recoveries in the range 82-100% (ovatoxins) and 59-72% (palytoxin) for samples at the highest spiking level when extracted with acidic or alkaline methanol:water mixtures. Deployment of this polymer in *O. cf. ovata* cultures demonstrated that polymers captured 6-time higher free ovatoxin levels as compared to a commercial resin. Molecular modelling of palytoxin fragments with native γ-CD suggest an interaction with both ends of the molecule as capture mechanism (Figure 1).

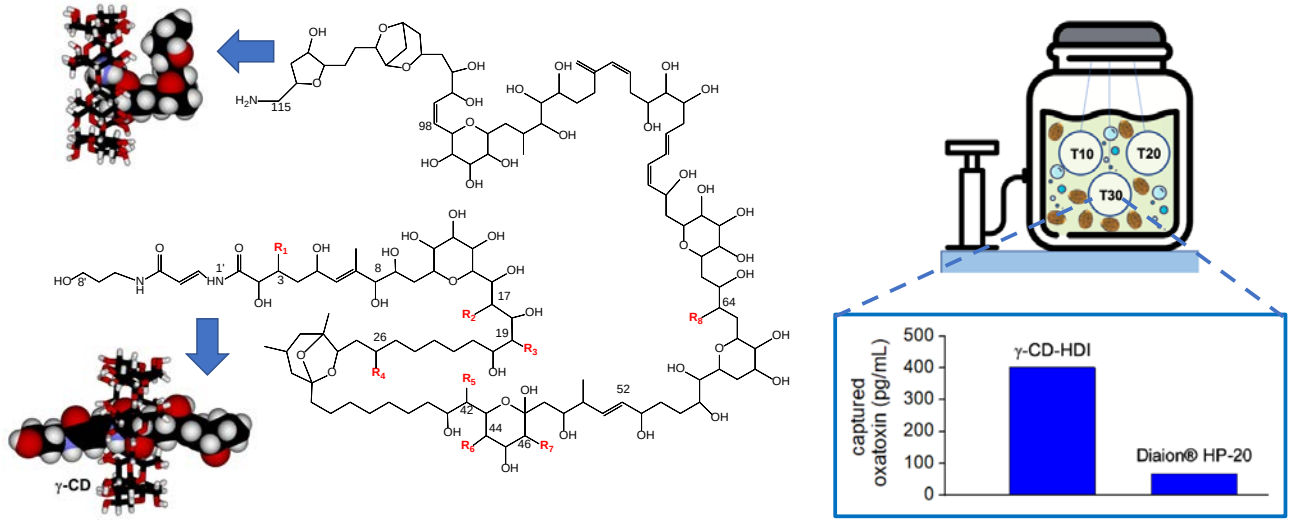

Figure 1. Toxin capture levels and molecular modelling of the γ-CD/palytoxin interaction.

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PP37

Carvedilol–Heptakis (2,6-di-O-Methyl)-β-Cyclodextrin Inclusion Complex: Compatibility with Excipients and Biological Studies

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Carvedilol (CARV), a prescribed antihypertensive agent as a treatment against chronic heart failure, left ventricular dysfunction following myocardial infarction and angina displays low water solubility, poor bioavailability as well as rapid first-step metabolism upon oral administration. Complexation with cyclodextrins is a valuable strategy for improving the physicochemical properties of drugs and its biopharmaceutical profile [1-3].

Development of supramolecular drug delivery systems has earned greater attention in view of their potential to improve drug solubility, stability and bioavailability. The current study aims to investigate the biological properties and excipient compatibility of the inclusion complex (IC) of CARV with heptakis(2,6-di-O-methyl)-β-cyclodextrin, in order to optimize its pharmaceutical performance. Towards the analysis of this newly formed compound, a series of physicochemical and biological assays were performed leading to the evaluation of the potential impact of pharmaceutical excipients on the supramolecular adduct. Compatibility studies between IC and starch, lactose, magnesium stearate and talc were carried out using various analytical techniques, including universal-attenuated total reflectance Fourier-transform infrared spectroscopy, powder X-ray diffractometry and thermal analysis for the identification of possible interactions. The study employed biological evaluations–including the Alamar Blue assay for antitumor activity and the DPPH radical scavenging assay for antioxidant capacity–to investigate the potential influence of the IC on CARV's bioactive properties.

Insights gained from this study provide valuable information for the development of optimized CARV/CD-based pharmaceutical products, contributing to the understanding of formulation stability and compatibility.

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PP38

Thermal studies on α-cyclodextrin

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Studying the thermal stability of alpha-cyclodextrin (ACD) is crucial for understanding its performance and reliability in various applications, since it is widely used in industries such as pharmaceuticals, food technology, and materials science [1]. Thermal stability analysis helps determine the conditions under which alpha-cyclodextrin maintains its structural integrity and inclusion capabilities, ensuring effective encapsulation, controlled release, or stabilization of guest molecules. Moreover, insights into its decomposition patterns and stability thresholds are essential for optimizing manufacturing processes, storage conditions, and shelf life, thus enhancing the safety and efficiency of products that incorporate this versatile oligosaccharide. According to this, we focused on investigation of thermal stability and kinetics of ACD decomposition under thermal stress in oxidative condition, at five heating rates β = 2, 4, 6, 8 and 10 °C·min^{-1}. The obtained data were processed according to the isoconversional methods of Friedman and Flynn-Wall-Ozawa (Figure 1).

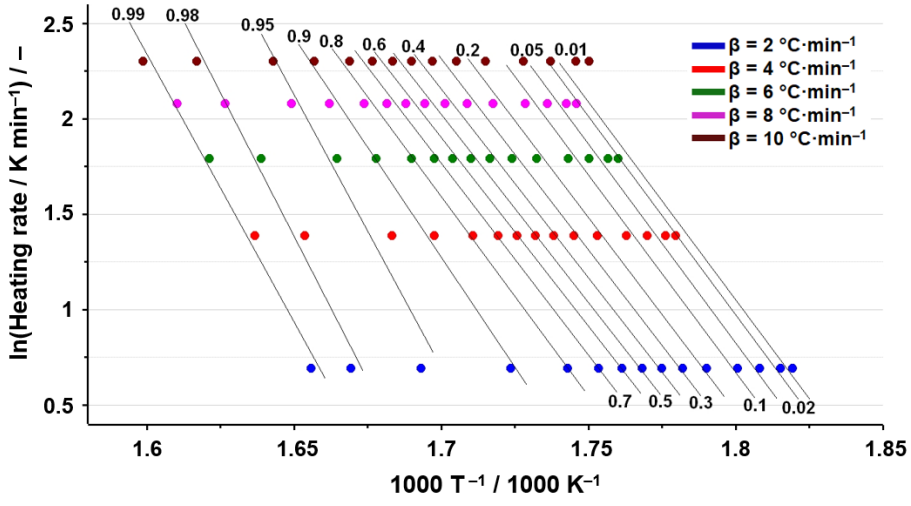

Figure 1. Flynn–Wall–Ozawa (FWO) plot

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Enhancing Curcumin's Nutraceutical Potential through Cyclodextrin Inclusion Complexes

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Cyclodextrins (CDs) are pharmaceutical excipients which possess a truncated cone shape with the outer part hydrophilic in nature providing them water-solubility, and the inner cavity hydrophobic, conferring them the ability to fully or partially capture a wide variety of compounds in a process known as complexation. They are versatile carriers for bioactive compounds derived from natural sources in various applications including drugs, food and cosmetics [1].

Curcumin (CMN), a polyphenolic compound derived from *Curcuma longa* is renowned for its potent antioxidant, anti-inflammatory, antiaging and anticancer properties. Despite its therapeutic potential, curcumin's poor aqueous solubility and low bioavailability limit its application as a nutraceutical [2]. CDs complexation has emerged as a promising strategy to overcome these limitations by enhancing curcumin's solubility, stability and bioavailability [3].

The encapsulation of CMN and piperine in hydroxypropyl-β-cyclodextrin (HP-β-CD) cavity resulted in an improve in CMN stability under simulated physiological conditions, solubility and biological activity. The inclusion complex (IC) was characterized by means of X-ray diffractometry, differential scanning calorimetry, spectroscopy and the biological efficiency was evaluated by assessing the inhibition of certain enzymes relevant in inflammatory and metabolic processes (e.g. acetylcholinesterase, butyrylcholinesterase). HP-β-CD has proved to be an effective carrier for curcumin-piperine nutritional systems, significantly improving the solubility, stability, biological activity (especially inhibition of key enzymes), thus providing a type of formulation that may have promising applications in the development of improved supplements or natural therapies [2].

Complexation of CMN with γ-cyclodextrin (γ-CD) demonstrated an important improvement in CMN bioavailability. The results of a human clinical trial in which participants received supplements containing CMN/γ-CD IC indicated a significant increase in plasma tetrahydrocurcumin levels, faster absorption and higher systemic exposure compared to plain CMN or other formulations. Also, the γ-CD protected CMN from premature degradation, facilitating its conversion to active metabolites [4].

These findings highlight the potential of CD to enhance the nutraceutical properties of curcumin, supporting the development of more effective dietary supplements and functional foods. Future research should aim to assess the long-term safety and efficacy across diverse populations.

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PP40

Organic-Inorganic platform for PFAS remediation through host-guest interactions

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Per- and polyfluoroalkyl substances (PFAS) are substances of significant concern, due to their human and ecological toxicity. Their massive use in industry and their persistence in environment led to their presence everywhere, from food packaging to drinking water or food [1]. There is thus a growing interest in developing green and innovative sequestration strategies for this kind of molecules, especially in solution. Among these, cyclodextrin complexation is emerging, due to their high affinity with different PFAS [2].

This work focuses on the green synthesis of a new organic/inorganic platform (represented in Figure 1) able to bind PFAS through host-guest interactions thanks to a cyclodextrin moiety grafted on porous silica. The silica matrix renders the material insoluble and should improve its depolluting properties by its ability to bind PFAS. To ensure a green process, mechanochemistry has been chosen to modify cyclodextrin and silica into reactive intermediates. The two moieties were then grafted together in solid phase to give the final material which has been fully characterized.

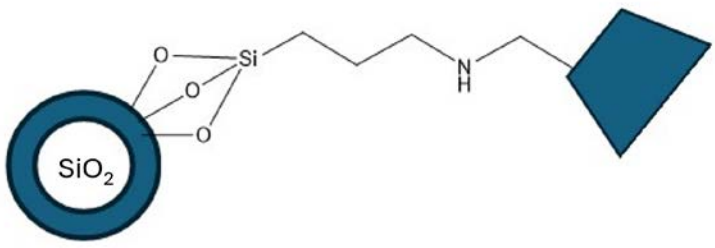

Figure 1. Graphical representation of the hybrid material

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Comparative Study of Hydroxypropyl-Chitosan and Cyclodextrin Polypseudorotaxan-Based Lacquers in Nail Disease Treatment

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Water-soluble lacquers have transformed the treatment of nail diseases, particularly onychomycosis, by enhancing drug penetration and bioavailability. Among the most innovative technologies are hydroxypropyl-chitosan-based lacquers and cyclodextrin polypseudorotaxanes-based lacquers, both of which improve drug interaction with the nail microstructure. This study aims to compare the efficacy of these two formulations in promoting the absorption of antifungal agents in the nail.

Cyclodextrins, particularly Hydroxypropyl-β-cyclodextrin (HPBCD) and Methyl-β-cyclodextrin (MBCD), act as effective nail permeation enhancers [1]. By increasing nail hydration and porosity, they facilitate greater diffusion of active ingredients without altering keratin's disulfide bonds. This unique mechanism enables cyclodextrins to encapsulate hydrophobic amino acids, reducing protein interactions and expanding the nail matrix. Consequently, ciclopirox penetration is significantly higher in lacquers formulated with pseudopolyrotaxane-cyclodextrins than in those based on hydroxypropyl-chitosan [2] In vitro and ex vivo studies have demonstrated superior drug concentrations within the nail matrix when using cyclodextrin pseudopolyrotaxane-based lacquers [1,2]. Clinical trials [3] further confirm their improved therapeutic performance, showing higher healing rates, better antifungal efficacy, and reduced recurrence compared to conventional treatments. Patients using these formulations have experienced prolonged protection against reinfection, reinforcing their potential as a more effective and sustainable alternative.

These findings highlight the advantages of water-soluble lacquers, particularly those incorporating cyclodextrin technologies, in optimizing transungual drug delivery. Their ability to enhance treatment outcomes positions them as a promising advancement in the management of nail diseases.

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PP42

A supramolecular assembly made of poly-sulfobutyl-β-cyclodextrin and a tetracationic Zn (II) porphyrin for antimicrobial photodynamic therapy

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The rise of multidrug-resistant (MDR) pathogens poses an increasingly critical challenge in the management of nosocomial infections. Conventional therapeutic treatments often fail due to bacterial resistance mechanisms, including biofilm production, which significantly impairs antibiotic efficacy [1]. Consequently, there is a strong requirement for innovative and more effective therapeutic strategies. In this context, Antimicrobial Photodynamic Therapy (aPDT) has emerged as a highly promising complementary approach [2]. aPDT involves the activation of photosensitizers (PSs) by visible (Vis) or near-infrared (NIR) light, resulting in the generation of cytotoxic reactive oxygen species (ROS), predominantly singlet oxygen ($^1O_2$). Within our ongoing research on nanophotosensitizers (nanoPS) based on cyclodextrins [3,4], we report here a novel supramolecular assembly based on a soluble sulfobutyl-β-cyclodextrin polymers (SBBCDPS) [5] and the zinc(II) derivative of 5,10,15,20-Tetrakis(1-methylpyridinium-4-yl)porphine tetrakis(*p*-toluenesulfonate) (ZnTMPyP). The assembly was fully characterized by UV/Vis, steady-state and time-resolved emission spectroscopies, Dynamic Light Scattering (size and ζ-potential measurements). Stability studies in biological relevant media were carried out to establish the suitability of SBBCDPS/ZnTMPyP assemblies in antibacterial photodynamic application against bacteria involved in fatal hospital-acquired infections.

Acknowledgements: This work was supported by the MUR-PNRR SAMOTHRACE (SiciliAn MicrOnanoTecH Research And innovation Center) ECS 00000022 and Programma Regionale SICILIA FSE+ 2021-2027, Priorità 2, ESO 4.7 ('Avviso pubblico n.15/2024) per il finanziamento di borse regionali di dottorato di ricerca in Sicilia

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Improving Quercetin Chemical-Pharmaceutical Profile Using Cyclodextrin-Based Nanosponges

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The nutritional and physiological effect of polyphenols is the reason for the growing research interest in flavonoids. Quercetin (2-(3′,4′-dihydroxyphenyl)-3,5,7-trihydrochromen-4-one) and its derivatives are among the most abundant polyphenols in plants where they can be found in different cell types, tissues, or parts of cells, shielding plants from oxidative stress, regulating cell growth and differentiation. There are able to amplify the effect of biologically valuable components and their positive impact on human health acting as antioxidant, antifungal, antibacterial and antiviral agents, preventing against age-related neurodegeneration and cancer.

Though quercetin is a lipophilic bioactive compound with numerous therapeutic uses, it appears to be difficult to use because of its poor solubility in aqueous medium and its lipophilicity. Several attempts to enhance quercetin bioavailability are cited in the literature, i.e. encapsulation and emulsification, attaching different sugar moieties to quercetin etc. [1,2].

We have studied the interactions between quercetin and cyclodextrin based nanosponges, such as carbonyl-diimidazole cross-linked cyclodextrin polymers compared to the inclusion complexes .

Cyclodextrin based nanosponges (CD-NS) and polymers, nanostructured cross-linked polymers, usually obtained by reacting cyclodextrin with various cross-linkers are interesting drug delivery systems as they are able to increase the dissolution rate, solubility, stability, and permeability of insoluble drugs and sometimes to provide controlled drug release [3,4].

The prepared nanosponges and their complexes with quercetin were characterized by FT-IR, SEM and thermal analysis. The solubilization efficiency, lipophilicity of the complex and the loading capacity were determined. Solubility studies were performed according to the method reported by Higuchi and Connors. The quercetin levels have been determined by UV spectrometry at 375 nm and the phase solubility diagrams plotted are AL type for the quercetin entrapped in polymers.

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Flavonoid- and anthocyanin-based lipopolyphenols: enzymatic synthesis, antioxidant activity and cyclodextrin complexes

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Flavonoids and especially anthocyanins from fruit extracts are highly hydrophilic, have low bioaccessibility (difficult to cross cell membranes), and easily metabolized/excreted. Moreover, they are not well molecular encapsulated by cyclodextrins (CDs) for enhancing properties.

The goal of the study was the enzymatic synthesis of flavonoid glycoside/anthocyanin-fatty acid (FA) bioconjugates using a "bio-click chemistry"-like technique applied to fruit extracts followed by cyclodextrin complexation for enhancing the bioconjugate water solubility and bioavailability/bioaccesibility of these new antioxidant compounds [1,2a]. Extracts from various fruits such as blueberries (*Vaccinium myrtillus*, *Vm*) or grapes (*Vitis vinifera*, *Vv*) were subjected to esterification with FAs using Novozym 435®, at 40 °C for 168 h. Further, the bioconjugate mixtures were complexed with natural CDs by co-crystallization [2b, 2c] (Figure 1). Both bioconjugate mixtures and CD complexes were evaluated for their antioxidant activity and DPPH· reaction kinetics, and characterized by HPLC, FTIR and thermal techniques. Statistically significant kinetic models (r^2 > 0.97 for the "fast and slow reaction" models, *Vm*-palmitic acid bioconjugates case) were obtained for both extracts and bioconjugate mixtures, but with higher half-time values for the last samples (with more than 20%), especially for 3th and 4th order kinetic models. In conclusion, the new hydrophobic bioconjugate mixtures can be encapsulated in CD efficiently and exhibit prolonged antioxidant effect.

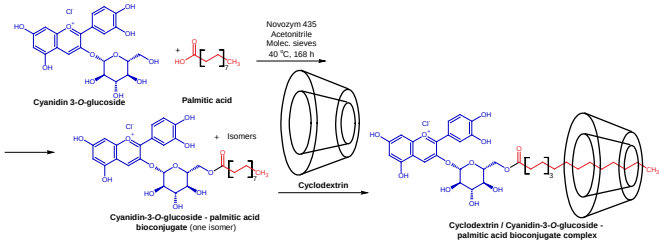

Figure 1. Schematic representation of the enzymatic synthesis of extract-based lipopolyphenol mixtures and cyclodextrin complexation (e.g. cyanidin-3-*O*-glucoside – palmitic acid bioconjugate).

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Design, drug loading, and characterization of a pyromellitic dianhydride–based β-cyclodextrin polymer

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Polymers are synthesized from native cyclodextrins with cross-linking agents like dialdehydes, epoxides, diacyl chlorides, carbonyldiimidazole, diphenyl carbonate, or organic dianhydride. Depending on the degree of crosslinking, polymers have different properties. For example, nanosponges are hyper crosslinked polymers with high porosity, insoluble in water that can include both hydrophilic and hydrophobic molecule structures used as drug delivery systems [1,2]. In literature there were also reported hydrophilic cyclodextrin based polymers crosslinked with epichlorohydrin, polycarboxylic acids, polyanhydrides and their properties were investigated against different therapeutic agents such as: antitumorals, antibiotics, antivirals and used as delivery systems [3-5].

This study aimed to prepare a β-cyclodextrin-based polymer using pyromellitic dianhydride as a cross-linking agent. The resulting polymer was physicochemically characterized by infrared (IR) spectroscopy, thermal analysis, particle size and polydispersity index (PDI) measurements via dynamic light scattering (DLS), and scanning electron microscopy (SEM). The molecular weight of the polymer was determined using Nanokin Software and following the thechnical instructions of the VascoKin particle analyser. Elemental analysis of the polymer was also performed.

The loading capacity of the polymer was investigated using various active pharmaceutical ingredients (APIs), including complexes aluminium and gallium complexes with 5-hydroxyflavone (with antitumoral properties) and oseltamivir (an antiviral agent). The loaded polymers were physicochemically characterized by infrared (IR) spectroscopy, thermal analysis, particle size and polydispersity index (PDI) measurements via dynamic light scattering (DLS) and scanning electron microscopy (SEM).

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Advancing UDP-003, a First-in-Class Therapeutic Targeting Oxidized Cholesterol to Reverse Atherosclerosis

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Cardiovascular disease (CVD) remains the leading global cause of death, with current therapies unable to fully address its progression. Cyclarity Therapeutics has developed a novel class of cyclodextrin-based therapeutics designed to eliminate 7-ketocholesterol (7KC), a cytotoxic oxidized cholesterol implicated in foam cell formation and plaque development. UDP-003, a dimerized and selectively engineered cyclodextrin, binds and removes 7KC from biological systems with high specificity. In vitro studies show its capacity to prevent and reverse foam cell formation, and in vivo testing confirms selective clearance of 7KC. IND-enabling studies in both rodent and swine models demonstrate a favorable safety profile with no CYP, transporter, or ototoxicity-related liabilities. UDP-003 is excreted unchanged in urine and shows no systemic metabolic burden. The first-in-human trial is ongoing in Australia, in partnership with the Victoria Heart Institute. UDP-003 represents a new disease-modifying approach in the treatment of atherosclerotic disease.

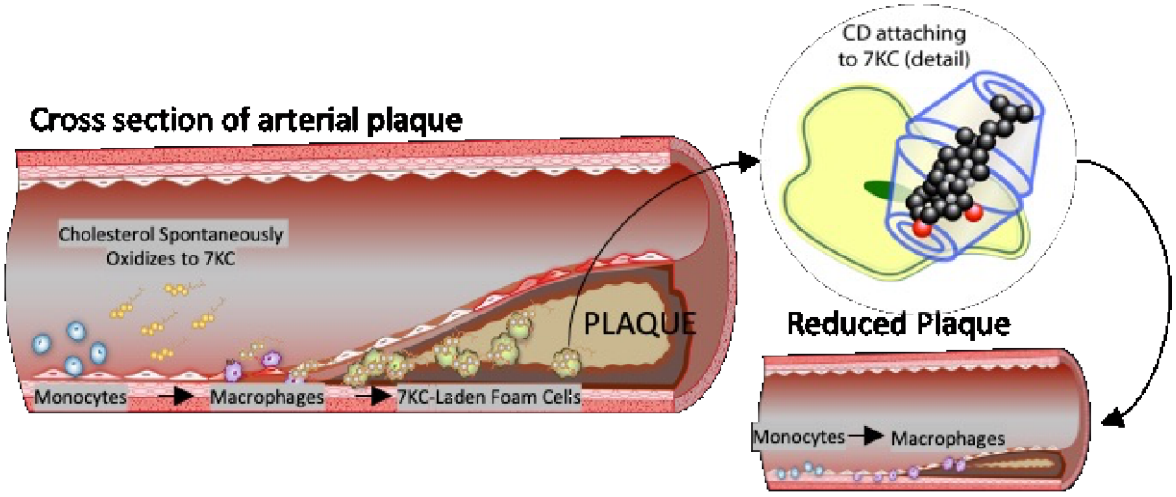

Figure 1. Atherosclerosis, 7KC, and CDs.

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Title Benefit of cyclodextrins for the bioproduction of 7-hydroxytropolone by Pseudomonas PA14H7: physicochemical studies and evaluation of the biological activity against "blackleg", a bacterial disease of potatoes

Achille Daguin[1], Sébastien Rigaud[1], David Mathiron[1], Serge Pilard[1], Euphrasie Munier-Lépinay[2], Mounia Khelifa[2], Miriana Kfoury[3], David Landy[3], Sylvain Laclef[4], Florence Djedaïni-Pilard[4]

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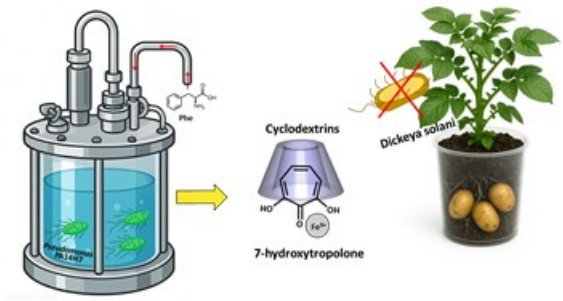
Cell-free supernatant (CFS) of the strain *Pseudomonas sp.* PA14H7 has shown interesting activity against *Dickeya Solani*, the main bacterial pathogen responsible of blackleg disease for potato. We reported that *Pseudomonas sp.* PA14H7 produces a metabolite, the 7-hydroxytropolone (7-HT), which acts as an iron chelator limiting the growth of the pathogens [1,2]. Recently, we identified phenylalanine (Phe) as a 7-HT biosynthetic precursor. Cyclodextrins (CDs) have already been used for their ability to form inclusion complexes with several guest molecules in culture media leading to an increase of the bioproduction of metabolites of interest, as reported for Resveratrol [3]. In this context, the current study explores the potential of CDs to improve 7-HT bioproduction and to enhance the CFS-*Pseudomonas sp.* PA14H7 biological activity. Preliminary physico-chemical studies (NMR, ITC) revealed stronger interactions of 7-HT with β-CD and RAMEB. The addition of this two CDs in a minimum culture media containing Phe led to an increase of 7-HT bioproduction and to a better antagonist activity against *Dickeya Solani*. These findings provide new insights for the use of Pseudomonas *sp.* PA14H7-CD formulation as a biocontrol agent.



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Bioactive Delivery through Quercetin – Cyclodextrin Inclusion Complexes in Dairy and Packaging Systems: A Nutraceutical Strategy

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Cyclodextrins (CDs) are cyclic oligosaccharides with a hydrophilic exterior and a lipophilic cavity, enabling the encapsulation of hydrophobic molecules. This enhances solubility and protects against degradation, supporting their use in food systems and bioactive delivery efficiency [1]. Quercetin (QUE), a flavonoid found in various plants possesses antioxidant, anti-inflammatory, anticancer, and antidiabetic properties, making it a promising nutraceutical ingredient. However, its poor water solubility and low bioavailability, limit its effectiveness, leading to the exploration of strategies to enhance its delivery and stability in food and pharmaceuticals [1,2]. Among these strategies, casein nanoparticles were developed to enhance QUE oral bioavailability, with 2-hydroxypropyl-β-CD associated in order to minimize presystemic metabolism by modulating efflux pumps and metabolic enzymes. This system exhibited an oral bioavailability nine times higher than QUE oral solution in a mixture of PEG 400 and water [2]. Solid inclusion complexes (IC) of QUE with β-CD and γ-CD show that γ-CD, with its larger cavity, forms a more stable complex. Antioxidant assays revealed that β-CD/QUE had the highest anti-peroxidation capacity, followed by free QUE and γ-CD/QUE. These complexes were successfully applied as nutraceutical additives in fresh cheese, improving texture and appearance without altering sensory properties [1]. The incorporation of cocoa-derived phenolic compounds, both free and encapsulated in CDs, was studied in fortified drinking yogurts. While free phenols, particularly QUE and gallic acid, increased antioxidant activity, CD-based complexes did not significantly enhance antioxidant properties or affect lactic acid bacteria viability during storage [3]. An innovative food packaging film incorporating β-CD/QUE IC into a matrix of tragacanth gum and carboxymethyl chitosan showed improved mechanical properties, reduced water vapor and oxygen permeability, and strong antioxidant activity, underscoring their potential in food preservation [4].These findings highlight the promise of CD IC in enhancing the QUE's nutraceutical potential, encouraging further research into optimizing complexation methods and assessing long-term stability, safety and efficacy.

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Industrial production of a rare Cyclodextrin utilizing a novel CGTase in *Clostridium Saccharoperbutylacetonicum*

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Cyclodextrins are cyclic oligosaccharides produced from starch hydrolysis using bacterial enzymes and are differentiated by the number of glucose units in the ring structure (typically 6,7 or 8 subunits). We have identified a novel cyclomaltodextrin glucanotransferase enzyme from *Clostridium saccharoperbutylacetonicum* that produces a smaller and pure cyclodextrin product. We report on improvements in gene expression and enzyme secretion in the native bacterial host and a fermentation route to produce the enzyme at scale. We also report on a new analytical method, based on LC-ESI-MS/MS, to detect small ring cyclodextrins. The enzyme was produced at scale and used to hydrolyse starch. We successfully demonstrated the production of a pure cyclodextrin composed of five glucose subunits (N5). Next, we plan to produce test samples for functional testing and industrial application.

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Systematic investigation of cyclodextrin-induced bioactivity mechanisms against *Candida albicans*

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The increase in the prevalence of fungal infections, coupled with increasing antifungal resistance, highlights the urgent need for novel antifungal agents. *Candida albicans*, the most prevalent human-pathogenic Candida species, has been shown to cause a wide spectrum of diseases, including cutaneous, mucosal, and systemic infections. Cyclodextrins (CDs) are frequently employed as excipients in antifungal formulations to improve the physicochemical properties and bioavailability of host molecules [1]. In our previous studies, we found that CDs may exert intrinsic fungicidal activity, even in the absence of a complexed antifungal agent [2]. Nevertheless, these cyclic oligosaccharides have not been the subject of systematic study with regard to their effects and bioactivity in the absence of a complex active substance. This presents a significant gap in our understanding, necessitating further research to reveal the mechanisms of action associated with its bioactivity.

The present study aimed to elucidate the mechanisms underlying the antifungal activity of cyclodextrins. We conducted a systematic investigation to identify how specific CDs influence the viability, reproduction, and physiology of *C. albicans*. Both native CDs and selected derivatives were tested over a concentration range of 0.1–12.5 mM in a dynamic system, considering both time- and dose-dependent effects. The main objectives of this study were threefold: (i) to assess the effect on viability by means of enzyme activity and cell number measurements; (ii) to assess the potential induction of reactive oxygen species (ROS) generation as a mechanism of antifungal action; and (iii) to examine the impacts of CDs on membrane integrity.

While membrane integrity remained largely unaffected by cyclodextrins, a substantial change in ROS production was detected. The extent of these effects was found to be influenced by several factors, including the contact time, the concentration and structure of the cyclodextrins. While the implications and functional consequences of these findings were not always clear, our results suggest that CD-induced ROS generation may contribute to their cytotoxic effects on *Candida albicans*.

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Optimization of the pharmaceutical efficacy of loratadine using cyclodextrin-based nanosponge encapsulation

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This study explores the potential of β-cyclodextrin-based nanosponges (CD-NSs) as encapsulating carriers for loratadine, a poorly water-soluble H1-antihistamine. Due to its limited aqueous solubility, the compound suffers from reduced oral bioavailability. The encapsulation into CD-NS offers a promising strategy to enhance solubility, stability, and controlled release behavior. NSs were synthesized by crosslinking β-CD with carbonyldiimidazole (CDI) in three molar ratios (1:4, 1:8, and 1:12). Drug loading was achieved via a homogenization technique, and encapsulation efficiency was determined through HPLC-UV analysis. Preliminary results for loratadine revealed exceptionally high encapsulation efficiency across all formulations, ranging from 98.88% to 99.76%, with minimal variance between molar ratios. These findings support the possibility of optimizing production costs by selecting lower crosslinker ratios without sacrificing performance. Thermogravimetric analysis (TGA) showed the degradation profile of encapsulated loratadine differing from the free drug, suggesting improved thermal protection and integration within the NS matrix. This structural stabilization is key to developing more effective and patient- friendly drug formulations. The CD-NS matrix acts as a porous three-dimensional system that enhances drug entrapment, protects compounds, and may facilitate controlled and prolonged release in physiological environments ultimately reducing side effects and improving therapeutic efficacy, for novel pharmaceutical formulations with improved solubility, stability, and bioavailability.

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Thermodynamics, molecular dynamics, and putative entrance mechanisms of 1-alkylsulfonates, alkyl sulfates and lipopeptides into the cyclodextrin cavity

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Cyclodextrins (CDs) are widely used macrocyclic host molecules that are known for their ability to form relatively stable complexes with a variety of lipophilic guest ligands. The stability of the resulting host–guest (cyclodextrin–ligand) inclusion complexes is mainly governed by non-covalent interactions, such as van der Waals forces, hydrogen bonds and dipole–dipole interactions. This phenomenon is used to modify the physicochemical properties of guest molecules, including their solubility, stability, reactivity, and biological activity. Consequently, cyclodextrins have a wide range of applications in various fields, including the food and pharmaceutical industries and the life sciences.

In this contribution, we present the physicochemical principles underlying the interactions of cyclodextrins (*α*-, *ß*- and *γ*-) with guest molecules representing different types of low-molecular-weight compounds such as 1-alkylsulfonates ($R\text{-}SO_3^-$) and alkyl sulfates ($R\text{-}O\text{-}SO_3^-$) [1] as well as with the series of lipopeptides representing the conjugation of the KR12 peptide ($K^{18}R^{19}IVQR^{23}IK^{25}DFLR^{29}\text{-}NH_2$), the smallest antimicrobial peptide derived from human cathelicidin LL-37 [2], with some fatty acid residues, namely octanoylated (C8-KR12-NH_2), laurylated (C12-KR12-NH_2) and myristoylated (C14-KR12-NH_2) KR12 peptide.

The thermodynamic parameters (ΔG, ΔH, $T\Delta S$) of the interactions obtained from isothermal titration calorimetry (ITC) experiments provided valuable insights into the molecular nature of the interactions. These findings were complemented by molecular dynamics simulations. Particular attention was paid to studying the correlation between the strength of the interactions and the structural features of the ligands, including the length of the hydrophobic moiety of the guest and the size of the cyclodextrin cavities. Furthermore, putative entrance mechanisms for ligands into the cyclodextrin cavities were proposed and discussed for the first time, giving a comprehensive view of the interaction processes.

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Theoretical exploration of sulfonylurea–β-CD complexes: role of substituents in stability and binding modes

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Type 2 diabetes mellitus is a major contributor to global mortality. While metformin is a first-line therapy, when glycemic targets are hard to meet, sulfonylureas (SU) are often prescribed as second-line agents [1]. Despite their clinical efficacy, most SU suffer from low aqueous solubility, improving solubility of SU via inclusion in cyclodextrins [2], is a key pharmaceutical goal. This work investigates β-CD complexes with tolbutamide and tolazamide, using combined theoretical methods. Classical molecular dynamics with GROMACS [3] revealed various stable conformations influenced by the orientation and nature of the substituents in the sulfonylurea moiety. Representative structures were identified by clustering and optimized at the M062X-GD3/ACP-6-31G* level [4-6] evaluating interaction and deformation energies.

Results demonstrate the crucial stabilizing role of SU substituents, not only by occupying the β-CD cavity but also by enabling competition between different binding orientations. Energy decomposition showed that stabilization arises from a balance between SU@β-CD interactions and structural deformation. Non-covalent interactions were analysed using quantum theory of atoms in molecules, emphasizing the relevance of interactions between the β-CD rims and SU, particularly hydrogen bonds and dispersive contacts, as key determinants of conformational diversity and complex stability.

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Water-Stable α-Cyclodextrin-Based mofs for Efficient Dye Removal from Wastewater

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The increasing release of synthetic dyes from textile industries into aquatic ecosystems represents a significant environmental concern, due to their toxicity, persistence, and resistance to biodegradation. In this context, the development of efficient, sustainable, and water-stable adsorbent materials is crucial. This work presents the evaluation of α-cyclodextrin-based Metal-Organic Frameworks (MOFs)**,** crosslinked with hexamethylene diisocyanate (HMDI)**,** as highly efficient adsorbents for environmental remediation. However, the MOFs formed by coordination with K^+ ions are typically water-soluble and lack structural stability. To overcome this limitation, HMDI was used as a crosslinking agent, resulting in a supramolecular network with enhanced water resistance and improved integrity under operational conditions. The physicochemical properties of the resulting crosslinked MOFs were thoroughly characterized using ATR-FTIR, DSC, TG, SEM, Zeta potential, and XRD analyses. While the non-crosslinked MOFs were highly soluble, the HMDI-crosslinked structure exhibited stable morphology**,** a Zeta potential of −15 mV**,** and a partially amorphous structure with reduced crystallinity and thermal stability. The adsorption performance was evaluated using Direct Blue-78 as a model pollutant of typical textile dye waste. The effect of various environmental parameter including pH, ionic strength**,** and temperature on the adsorption efficiency was investigated. The results demonstrated that electrostatic interactions, along with salting-out effects, played key roles in the adsorption mechanism. Thermodynamic analysis revealed the process to be spontaneous and endothermic, with an increase in entropy**,** suggesting a disorder-driven adsorption mechanism. Adsorption isotherms (Langmuir, Freundlich, Temkin, and Dubinin–Radushkevich) indicated multilayer adsorption with non-uniform energy distribution across adsorption sites. Furthermore, kinetic studies using pseudo-first and pseudo-second order models confirmed the complexity of the process. The crosslinked MOFs exhibited a high adsorption capacity of 75 ± 5 mg/g, making them promising candidates for practical wastewater treatment applications.

Keyword: Metal-organic frameworks, hexamethylene diisocyanate, α-cyclodextrins, Textile dyes, Adsorption