7th George Olah Conference

XXIII Conference of the George Olah Doctoral School

29 September 2025

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Program

EVENT VENUE: BME CH201 ROOM PUNGOR

8^{30} Opening

ORAL PRESENTATIONS

Chairwoman: Emília Csiszár

8^{35}-9^{05} **Kata Enikő Decsov** – Environmental Challenges in Flame Retardance – Invited lecturer, George Olah Prize winner in 2024

9^{10}-9^{45} **János Korbuly** – Manufacturing of vaccines for veterinary purposes – Invited lecturer from Ceva-Phylaxia Plc., Head of Pilot plant

9^{45}-10^{05} **Diána Balogh-Weiser** – Development of nanocarriers for advanced formulation of therapeutic enzymes – Invited lecturer from the Department of Organic Chemistry and Technology

10^{05}-10^{25} Coffee Break

Chairman: László Nyulászi

10^{25}-10^{45} **Kinga Nyíri** – Antirepressor specificity is shaped by highly efficient dimerization of the staphylococcal pathogenicity island regulating repressors: Stl repressor dimerization perturbed by dUTPases – Invited lecturer from the Department of Applied Biotechnology and Food Science

10^{45}-11^{05} **Zsolt Kelemen** – The magical world of carboranes – Invited lecturer from the Department of Inorganic and Analytical Chemistry

11^{05}-11^{25} **Márton Körösi** – Experimental determination of solid-liquid-gas equilibria in high-pressure CO_2 – Invited lecturer from the Department of Chemical and Environmental Process Engineering

11^{25}-11^{45} **Róbert Várdai** – Recycling of Multilayer Soft Plastic Waste: Mechanical Properties and Feasibility – Invited lecturer from the Department of Physical Chemistry and Materials Science

11^{45}-12^{30} **László Homolya** – How do our body's bouncers operate? (Cell polarity and protein trafficking) – Invited lecturer from HUN-REN Research Center for Natural Sciences, Institute of Molecular Life Sciences

12^{30}-14^{00} Break and Poster session – 2nd floor

Jury: Mónika Molnár, Kata Enikő Decsov, László Nyulászi

P01	Anikó Boros	Comparison of methodologies for colour measurement in fresh chicken breast fillets under different storage temperatures
P02	Anna Matkovits	Identification of Climate Change Predictive Parameters in Hungarian Acacia Honeys
P03	Balázs Kenéz	Development of nanocellulose-based carriers for immobilization and purification of recombinant enzymes
P04	Dániel Fekete	Continuous twin-screw wet granulation using potassium sodium tartrate tetrahydrate
P05	Emanuela Cullhaj	Characterization of polymeric films for mucoadhesive drug delivery.
P06	Ghazwan Saleh Ahmed	Phase equilibrium and density measurements for the system methyl acetate + sunflower oil + carbon dioxide
P07	Gyöngyvér Pusztai	Thiadiazino-indole, thiadiazino-carbazole and benzothiadiazino-carbazole dioxides: synthesis, physicochemical and early ADME characterization of representatives of new tri-, tetra- and pentacyclic ring systems and their intermediates
P08	Imre Romsics	Reactive compatibilization of immiscible PLA/PBAT biopolymer blends for medical application
P09	Judit Erzsébet Budai	Chemical Recycling of Flexible Polyurethane Foams by Glycolysis: Toward a More Sustainable Polyol Recovery
P10	Kata Szayly	Characterization of mucoadhesion of polymer tablets on the surface of poly(vinyl-alcohol) hydrogels
P11	Kristóf Noel Garami	Target Agnostic Photoaffinity Labelling by Sulfonylhydrazones
P12	Máté Gergő Honvári	Enantiocomplementary Bioreduction of Flexible Ring N-(3-Oxobutyl)-Heterocycles Providing Enantiopure Chiral Fragments for Drug Discovery
P13	Máté Laurinyecz	Development of a Reusable MNP-Based Support for His-Tagged Enzyme Immobilization
P14	Medárd Koncz	Comparison of the stabilizing effects of ellagic acid and gallic acid in polyethylene
P15	Mihály Hegyi	Taylor Dispersion Analysis at High Pressure – Challenges and Corrections
P16	Noor Al Deeb	Quantum Chemical Insight into the Production of Reactive Oxygen Species by Catechol/o-Quinone Redox Cycling: The Case of 4-Hydroxyestrogens
P17	Péter Szemesi	Continuous-flow synthesis of aripiprazole through the safe utilization of THF hydroperoxide
P18	Zoltán Petrovics	Statistical assessment of content uniformity testing using conventional and process analytical technology -based analytical methods

STUDENTS' ORAL PRESENTATIONS

Section A – CH201

Chairman: László Poppe

14^{00}-14^{15} **Gergely T. Solymosi** – Unique potentiometric behavior of ion-exchanger nanopores

14^{15}-14^{30} **Apoko Stephen Omondi** – Tuning the photoluminescence response of doped zinc aluminate phosphors

14^{30}-14^{45} **Ziyoda Ganieva** – Ligand-Directed Cu_2O Shell Growth on Gold NanoPrisms: Surface Selectivity and Growth Mechanism

14^{45}-15^{00} **Lucy Nyambura Karanja** – Hydrothermal Carbonization of Spent Coffee Grounds into Hydrochar for Adsorptive Removal of Rhodamine 6G

15^{00}-15^{15} **Rudolf Mihály Mátyás** – Effect of the reaction conditions on the optical properties of Mn-doped spinel nanostructures

15^{15}-15^{30} **Meng Yang** – Addition reactions of phosphorus-centered radicals onto olefins: DFT and ab inito calculations

15^{30}-15^{50} Coffee Break

Section B – CH201

Chairman: Zsolt Kelemen

15^{50}-16^{05} **Kata Takács** – Synthesis, Evaluation and Concentration Effects of a Novel Natural-Based Phosphine Antioxidant in the Thermal Stabilization of Polyethylene

16^{05}-16^{20} **Petra Kántor** – Subcritical hydrolysis: a route from waste to raw material

16^{20}-16^{35} **Zsolt Szalóczy** – Reconciling Economic Growth and Sustainability: Is a Balance Possible?

16^{35}-16^{50} **Anna Péter-Haraszti** – Quantification of amorphous traces in crystalline carvedilol using different analytical methods

16^{50}-17^{05} **Viktória Berta Perey-Simon** – Impact of Genomic Uracil on Zebrafish Embryonic Development

17^{05}-17^{20} **Bálint Kurucz** – Resveratrol's effect on a mAb producing CHO cell line

17^{35} Closing – CH201

Abstracts of invited lectures

Development of nanocarriers for advanced formulation of therapeutic enzymes

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Enzyme-based therapies have emerged as key interventions for a wide range of medical problems, with over 100 therapeutic enzymes accepted for usage. These enzymes have an important role in treating a variety of disorders, including metabolic diseases, lysosomal storage disorders, and dermatological conditions. Among enzyme-based treatments, enzyme replacement therapies (ERT) involve the administration of specific enzymes that are either weak or absent in the human body in order to cure existing deficiencies or prevent consequences. Enzymes have excellent efficiency and selectivity but poor structural and functional stability. Environmental factors (temperature, solvent composition, pH, compounds with potential inhibitory effects, etc.) may result in considerable activity loss. Thus, the therapeutic use of native, solubilized enzymes has significant limits. To improve enzyme stability and activity, the use of solid carrier systems can provide new opportunities. However, standard formulations usually rely solely on small molecules, ignoring critical factors such as enzyme stability, dynamics, and size. Our study focuses on the development of nanocarriers, such as nanoparticles or nanofibers, which are applied to formulate therapeutic enzymes. Magnetic nanoparticle-based enzyme immobilization is a promising technique for improving enzyme efficiency in formulations. In our research, we aimed to develop a human tyrosine hydroxylase (hTH)-based ERT for the effective treatment of neurodegenerative illnesses with dopamine reliance. We observed significant improvements in stability and activity recovery after optimizing hTH immobilization using surface-modified magnetic and silica nanoparticles, indicating prospective pathways for therapeutic intervention in neurodegenerative conditions.[1] We have also worked on developing per os ERTs for digestive disorders using electrospun nanofiber-based lipase compositions. We continuously increased enzymatic activity and stability in GI fluid simulations by carefully optimizing fiber synthesis parameters and precursor properties.[2] Furthermore, we investigate nanofibrous formulations for enzyme-based topical treatments. We created a multi-layered nanofibrous face mask by mixing two lipases of different origin with a co-formulated antibiotic drug, Nadifloxacin. In our study, we discovered that electrospinning significantly increased lipase activity in skin lipid hydrolysis, allowing for effective delivery of Nadifloxacin from the nanofibrous mask to the epidermis. This study may provide the groundwork for a novel approach to treating problems including acne and inflammation.[3]

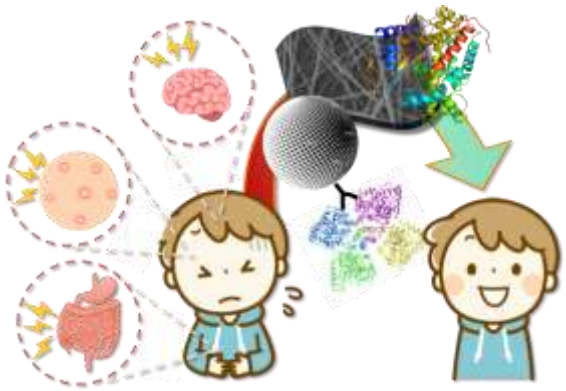

Figure 1. Application of nanofibers and nanoparticles in the formulated therapeutic enzyems – as a promising therapeutics for digestive problems, skin diesease and neurodegenerative disordes.

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Antirepressor specificity is shaped by highly efficient dimerization of the staphylococcal pathogenicity island regulating repressors: Stl repressor dimerization perturbed by dUTPases

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Pathogenicity islands in Staphylococci are regulated by Stl repressors that form strong dimers. It has been recently shown that SaPIbov1-Stl dimers are separated during the activation of the Staphylococcus aureus pathogenicity island (SaPI) transcription via helper phage proteins[1]. To understand the mechanism of this regulation, a quantitative analysis of the dimerization characteristics is required. Due to the highly efficient dimerization process, such an analysis has to involve specific solutions that permit relevant experiments to be performed. In the present work, we focused on two staphylococcal Stls associated with high biomedical interest, namely Stl proteins of Staphylococcus aureus bov1 and Staphylococcus hominis ShoCI794_SEPI pathogenicity islands. Exploiting the interactions of these two Stl proteins with their antirepressor-mimicking interaction partners allowed precise determination of the Stl dimerization constant in the subnanomolar range[2].

We showed at the first time that the strong interaction within the Stl repressor dimer dramatically interferes with the measurement of repressor:antirepressor equilibrium binding constant. Our results thus propose a generally applicable experimental approach to study other similar complexes.

We have revealed that only an intricate, fine-tuned interaction network between repressor:antirepressor complexation can adeptly compete with the highly efficient dimerization of the Stl repressors[3,4]. Interestingly the antirepressor proteins in some specific cases are dUTPase enzymes and thus the co-evolution of SaPIs and phages has provided us with an efficient dUTPase inhibitor, which can potentially be applied to study the cellular function of dUTPases.

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[2] Nyíri, K.; Gál, E.; Laczkovich, M.; Vértessy, B. G. *Sci. Rep.* **2024**, *14* (1), 1953.
[3] Kőhegyi, B.; Tóth, Z. S.; Gál, E.; Laczkovich, M.; Benedek, A.; Vértessy, B. G.; Nyíri, K. *Sci. Rep.* **2025**, *15* (1), 4836.
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The magical world of carboranes

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Do magical compounds exist that can be used as catalyst, biosensors, doping agent of conductive polymers, nuclear waste remediation, in cancer therapies or even in space technology? Although three-dimensional carborane clusters do not have any magical properties, their exceptional thermal and chemical stability, tailorability, ambiphilic character and unusually low toxicity or biocompatibility provide performance superior to that of conventional materials. Our group aims to understand and develop new carborane-based materials, which might find applications as light emitting materials or as potential boron neutron capture therapy agent. Apart from fluorescent materials[1] we investigate more fundamental aspects of carboranes, such as possible bond modulation[2] and the possible interaction between three dimensional carborane cluster and two dimensional ring systems.[3–6]

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Experimental determination of solid-liquid-gas equilibria in high-pressure CO_2

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Although supercritical carbon dioxide has widely known industrial applications such as supercritical fluid extraction of the decaffeination of coffee, a variety of phenomena related to this alternative solvent are still intensively researched, including studies on phase equilibria. High-pressure solid-liquid-gas equilibrium data may have significant importance in the early design of different procedures. The melting temperature of most solids increase with an increase in static pressure. Carbon dioxide pressure, however, has a different effect. By dissolving in the solid phase and/or the melt, it causes the melting temperature to decrease, up to a pressure where the effect is countered by that of static pressure. [1]

Experimental determination of melting properties in pressurized media is a specialized task, often conducted with individually developed methods. Procedures based on visual observation are often applied. [2–4] High-pressure view-cells, such as the one shown in the left panel of *Figure 1.*, offer the advantage of noticing signs of decomposition at the cost of human error in the detection of the phase-change.

Recently a measurement device (right panel of *Figure 1.*) and method has been developed aiming automated operation and the elimination of the operator's error. [5] A sample-filled cell and an 'empty' reference cell are pressurized and then heated identically. As the phase transition of the sample is often accompanied by a volumetric change, the pressure of the two closed cells start to differ. This is recorded using a differential pressure – transmitter.

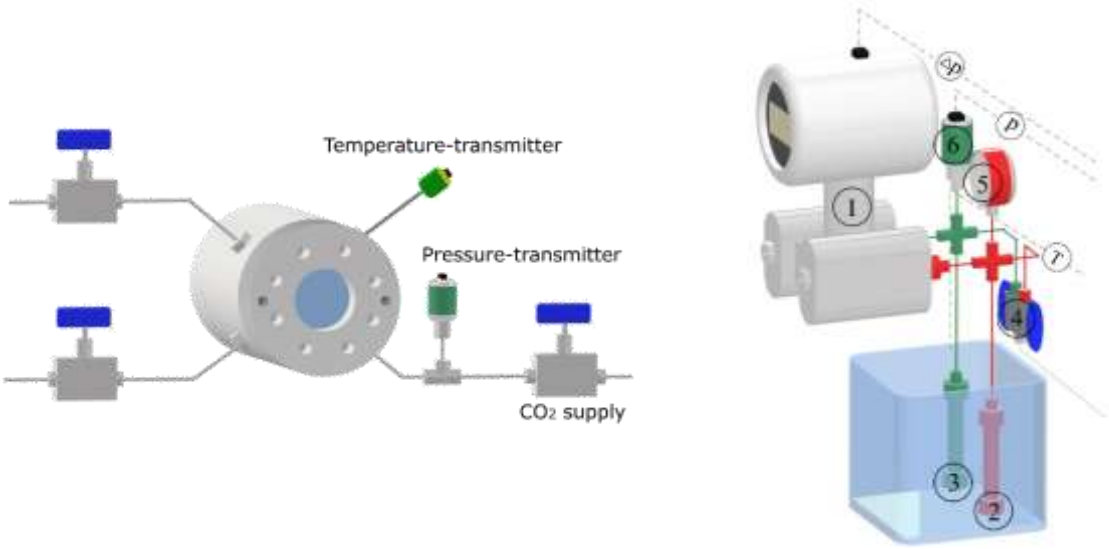

Figure 1. Schematic depiction of a high-pressure view-cell (left) and that of the measurement device based on volumetric changes (right). 1: differential pressure–transmitter; 2: reference cell; 3: sample holder; 4: valve; 5: pressure gauge; 6: pressure-transmitter

Highly crystalline organic samples, such as racemic ibuprofen and ketoprofen (*Figure 3.*) could be investigated with both methods, up to 30 MPa pressure. With well-defined, sharp melting signals, they were ideal candidates in verifying the new apparatus.

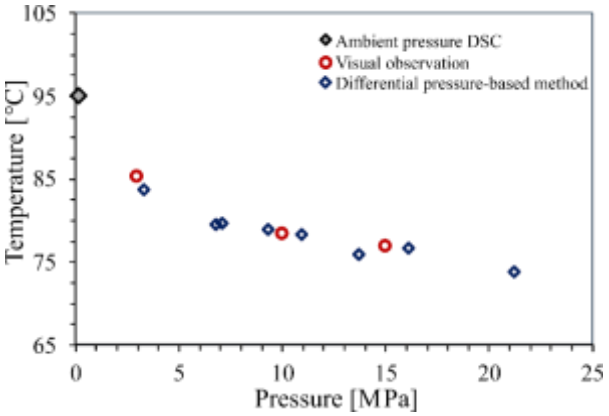

Figure 3. High-pressure melting behavior of ketoprofen

Investigated ionic liquids – tetrabutylammonium-halides –, however did not show significant volumetric change. But, their melting point depression could clearly be observed visually. The maximal melting point depression values decreased in the order iodide to chloride from approx. 34 °C to 9 °C. [6] Polymers have also been studied: both polycaprolactone and polyethylene glycol showed significant decrease in their melting temperature. Their composites with APIs may exhibit eutectic behavior.

The melting point depression phenomenon has already been made use of. Polymers subjected to carbon dioxide pressure may be processed at lower temperature, reducing thermal stress during extrusion. Besides its use as a temporary plasticizer, carbon dioxide has also been introduced to replace conventional foaming agents. Another interesting procedure, *particles from gas-saturated solutions* (*PGSS*) [7], serves the formation of particles in the micrometer size-range, with a narrow particle size distribution. In this process, a melt, in equilibrium with a pressurized carbon dioxide phase is formed. Then, it is sprayed to ambient pressure resulting in the fine powder. It can also be used to from composites. The above processes demonstrate the need for solid-liquid-gas equilibrium information, henceforth mentioned as high-pressure melting temperature data.

The support of the National Research, Development and Innovation Office (NKFIH) (OTKA PD_23 146145) is gratefully acknowledged. I owe special thanks to Edit Székely for her advice and the fruitful conversations, Dóra Arany, and all of the members of the High-Pressure Unit Operations Research Group for their dedicated involvement and work.

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Recycling of Multilayer Soft Plastic Waste: Mechanical Properties and Feasibility

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[2] *Laboratory of Plastics and Rubber Technology, Department of Physical Chemistry and Materials Science, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, Műegyetem rkp. 3., H-1111 Budapest, Hungary*
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The goal of our study was to recycle flexible multilayer food packaging films, because the majority of this type of plastic waste is incinerated or landfilled [1]. Since the components of multilayer films – mostly polyamide and polyethylene – are immiscible and incompatible, the recycling or the production of value-added products is difficult. Several attempts were made in order to improve the interfacial adhesion between the components by adding a coupling agent [2,3], however, the compatibilizers provided only a slight improvement. Our proposed solution is to use glass fiber with an appropriate surface coating as a reinforcement for the preparation of composites from the polymer blend of plastic waste. The multilayer packaging waste used in the research contains more polyamide than polyethylene. Therefore, we used two grades of glass fiber with different sizings, one for polyamide and one for polyethylene. In order to homogenize the glass fiber and the components of the film an extrusion step was applied. In the next step, standard specimens were injection molded, and then mechanical tests and calculations were performed to determine the applicability and price of the composites. The surface treatment of the glass fiber has a significant influence on the properties of the composites produced from plastic waste. The mechanical properties are not significantly different from those of glass fiber reinforced polyamide composites available on the market prepared from virgin polymer material. In the case of tensile strength and impact resistance, the sizing of the glass fiber is more emphasized. Composites containing fibers with sizing to polyamide perform outstandingly, considering that they are made from multi-component waste material, these results are remarkable. The implementation of our solution is feasible technologically; the mechanical properties of the product are comparable to high-performance grades available on the market, and its price is very favorable. The results of this research could contribute to the value-added recycling of plastic waste.

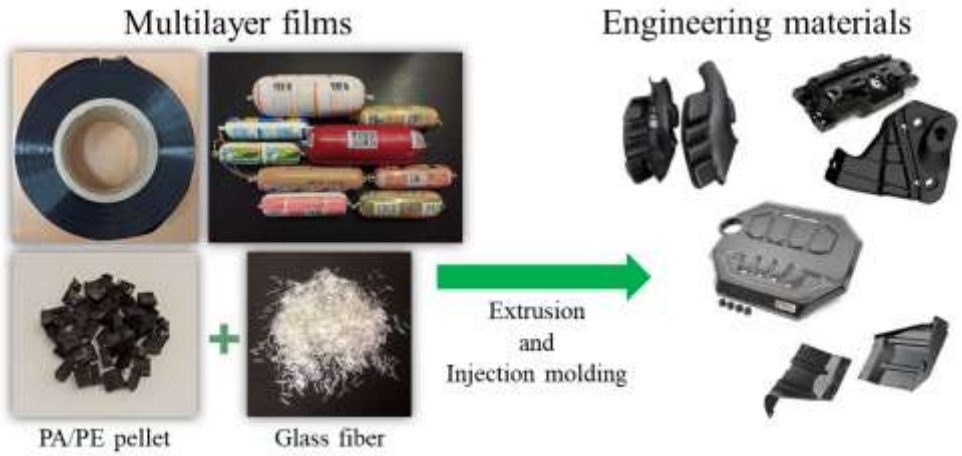

Figure 1. Value-added recycling of multilayer soft plastic waste.

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Abstracts of students' lectures

UNIQUE POTENTIOMETRIC BEHAVIOR OF ION-EXCHANGER NANOPORES

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Monitoring body hydration levels is key to enhancing the performance and protecting the health of athletes and people working in extreme heat. This could be achieved through the continuous and reliable on-skin measurement of the total ion concentration of human sweat, which would require a small and flexible, universal (i.e., non-selective) ion sensor that can be integrated into wearable platforms. While conductometry is widely used as a universal ion sensor due to its non-selectivity, it is strongly affected by cell geometry, temperature, and viscosity changes, hindering its application for on-skin monitoring. Potentiometry, on the other hand, is well-suited for wearable sensor systems, given its independence of cell geometry and viscosity, and its weak temperature dependence.

Conventional potentiometric sensors are based on plasticized PVC ion-exchanger membranes, which are unsuitable for total ion concentration measurements due to their inherent preference for more lipophilic ions over hydrophilic ones. This intrinsic selectivity pattern, known as the Hofmeister series, arises because ions are required to shed their hydration shells as they transfer into the hydrophobic polymer membrane. As human sweat contains in significant quantities several ions with substantially different hydration energy (e.g., potassium and sodium), plasticized PVC membranes are incapable of accurately measuring sweat total ion concentrations. The likely presence of highly lipophilic contaminants such as certain lipids and drug metabolites, which can affect the potential response of hydrophobic polymer membranes even at trace levels, further limits the accuracy of conventional potentiometric sensors. In addition, liquid membranes based on high-viscosity organic solvents like plasticized PVC are inherently *not* biocompatible.

Here, we show that non-selective and biocompatible potentiometric sensors capable of accurate total ion concentration measurements can be constructed by replacing hydrophobic plasticized PVC membranes with hydrophilic solid-state nanopore membranes. Hydrophilic nanopore membranes with electrically charged surfaces had been shown to act as effective permselective filters[1], producing concentration-dependent membrane potentials, without discriminating ions based on their hydration energy[2,3]. We fabricated hydrophilic anion- and cation-exchanger solid-state nanopore membranes by decorating the surface of gold nanopore membranes[4,5] with thiol-bearing sulfonate and tetraalkylammonium derivatives, respectively. We show that these hydrophilic ion-exchanger nanopore membranes can be used to potentiometrically measure sweat total ion concentrations with similar accuracy to conductometry but with much better robustness to temperature and viscosity changes. Unlike conventional potentiometric membranes, the potential response of hydrophilic nanopore membranes was unaffected by trace levels of highly lipophilic contaminants.

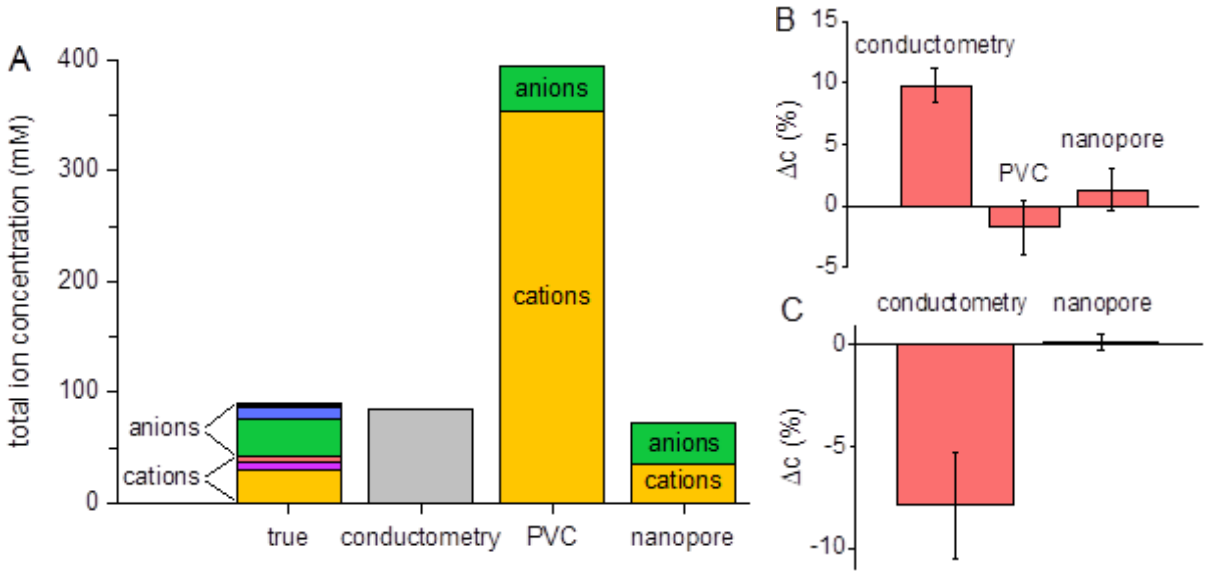

*Figure 1. **(A)** Determination of total ion concentration of a human sweat-like sample using conductometry, plasticized PVC membrane-based, and nanopore membrane-based potentiometry. The sample mimicked the median ionic composition of human sweat. The sensors were calibrated with pure NaCl standard solutions and then used to measure the total ion concentration of the multicomponent sample. During potentiometry, the total anion and cation concentrations were determined separately using anion- and cation-exchanger membranes. **(B)** Relative change in the measured total ion concentration caused by a temperature change of +5 °C. **(C)** Relative change in the measured total ion concentration caused by a viscosity change of +0.5 mPas induced by adding 14 mg/mL PEG to the sample.*

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TUNING THE PHOTOLUMINESCENCE RESPONSE OF DOPED ZINC ALUMINATE

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Spinel oxides have been in the focus of research as intrinsic luminescent materials or as hosts to luminescent centers when doped with rare earth or transition metal ions. Over the years, phosphors based on gallium and rare earth elements as dopants have been extensively investigated.[1] However, their cost and toxicity concerns have raised the need to seek alternatives that are benign and less costly to realize a similar luminescent response.[2] Garnite, a spinel oxide of the form AB_2O_4 in which A represents Zn^{2+} occupying tetrahedral sites and B, Al^{3+} occupying octahedral sites, is a wide band gap semiconductor with attractive physico-chemical properties.[3] It is currently being investigated as a host material for luminescent centers when doped with both manganese and chromium ions to generate a broad spectral and persistent luminescence in the Vis-NIR region.

The aim of this work is to synthesize singly doped and co-doped zinc aluminate phosphors, that can be selectively excited by UV-Vis to luminesce in a given section of the spectrum or produce multimodal emission with radiation of higher excitation energy, like X-rays. This aspect has not been adequately investigated, and as such, this work and its progress endeavor to extensively investigate the optical properties of luminescent zinc aluminate that emits radiation in three regions of the Vis-NIR spectrum. The hydrothermal synthetic protocol is implemented as it ensures great homogeneity of the synthesis precursors, as well as mild reaction temperatures, as opposed to other methods (solid state). Samples are then annealed at different temperatures to adjust their final crystallinity and to create defects, vacancies, and traps that are responsible for optical properties.

Manganese and chromium-doped zinc aluminate phosphors were synthesized, followed by annealing treatment at 600, 900, and 1100ºC. XRD and SEM-EDS were used to structurally and morphologically characterize the samples. From these analyses, it is evident that the dopant ions are successfully introduced into the host matrix without interfering with its crystallinity. Morphological characterization by SEM-EDS revealed irregular ellipsoidal particles with non-uniform shapes in all analyzed samples. EDS was employed to determine the precise elemental composition of the spinel structure. The results are consistent with the precursor composition used during the synthesis of the phosphors and confirm the incorporation of dopants at low atomic percentages, as expected given the millimolar concentration regime. Vibrational characterization was performed using Raman spectroscopy with 532 nm laser excitation. The observed vibrational bands centered at 420 cm^{-1} and 660 cm^{-1} are attributed to tetrahedrally and octahedrally coordinated ZnO and Al_2O_3 units within the $ZnAl_2O_4$ spinel, respectively, confirming the successful formation of the host spinel structure. This result is further supported by XRD analysis, which shows that all diffraction peaks correspond to single-phase crystalline $ZnAl_2O_4$, with no impurity-related phases detected. These findings indicate that Mn and Cr dopants effectively diffused into the spinel lattice without disrupting its crystallinity. Furthermore, the most intense diffraction peak, indexed as (311), shifts toward lower 2θ values

with increasing dopant concentration. This shift is attributed to lattice expansion caused by differences in the ionic radii of the host and dopant ions in both tetrahedral and octahedral sites.

X-ray Excitation Optical Luminescence (XEOL) and Photoluminescence Spectroscopy (PL) have been used to monitor the optical response upon excitation by X-rays and UV-Vis, respectively. Electron paramagnetic resonance (EPR) spectroscopy has been used to investigate the symmetry and environment around the luminescent centers and to provide a background for elucidating the observed optical behavior. X-band EPR spectra recorded at room temperature exhibited a well-defined sextet hyperfine splitting characteristic of Mn^{2+}. For chromium-doped samples, the EPR spectra revealed contributions from two distinct chromium species: (i) isolated Cr^{3+} ions in octahedral ligand environments, observed at lower magnetic field values with higher g-tensor values, and (ii) Cr–Cr ion pairs, responsible for weaker EPR signals at higher magnetic field regions with lower g values.

Photoluminescence (PL) studies demonstrated that electronic transitions of Mn^{2+} ions in tetrahedral sites of $ZnAl_2O_4$:Mn phosphors give rise to green emissions centered at 510 nm under UV–Vis excitation. In chromium-doped samples, a broad multi-peak emission is observed, including the R and N lines at 687 and 698 nm, respectively, as well as Stokes and anti-Stokes phonon sidebands, which are attributed to Cr^{3+} ions in perturbed and unperturbed octahedral environments. Substitution of Al^{3+} by Cr^{3+} generates new octahedral arrangements, with Cr^{3+} electronic transitions producing several narrow emission peaks between 667 and 740 nm. In co-doped $ZnAl_2O_4$ samples with significant chromium content, the green emission of tetrahedrally coordinated Mn^{2+} overlaps with the Cr^{3+} excitation band at ~530 nm. This overlap leads to quenching of the Mn^{2+} emission via resonance energy transfer.

Under X-ray excitation, intense emissions are observed, with Mn and Cr occupying distinct lattice positions within the spinel structure. The green emission at ~515 nm originates from Mn^{2+} in tetrahedral sites, while a broad NIR emission centered at 850 nm is attributed to transitions of Mn^{2+} ions located in octahedral sites. Cr^{3+} ions contribute a multi-peak emission spanning 679–712 nm. This transition is responsible for the observed persistent luminescence. The combined NIR emission from octahedrally coordinated Mn^{2+} and the red–NIR emission from Cr^{3+} fall within the biological optical window, where tissue transparency is maximized. This property renders the photoluminescent nanoparticles highly suitable for autofluorescence-free bioimaging and therapeutic applications, including photodynamic therapy.

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Ligand-Directed Cu_2O Shell Growth on Gold NanoPrisms: Surface Selectivity and Growth Mechanism

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Metal–semiconductor hybrid nanostructures are powerful tools for manipulating light-matter interaction at the nanoscale. In particular, Au/Cu_2O systems combine the plasmonic activity of gold with the photocatalytic potential of cuprous oxide.[1] To simultaneously take advantage of the photoexcitation determined charge separation between the Au and the Cu_2O domains and the large plasmonic near-fields at metal nanoparticles in general, region selective deposition of Cu_2O on the plasmonic nanoparticles would be necessary. To realize such a structure, we elaborated a ligand-assisted, region-selective surface energy modulation based synthesis strategy, enabling the preparation of of partial Au/Cu_2O core/shell nanoparticles, in which the tips of the gold nanoprisms remain exposed.[2] Gold nanoprisms of 75±6 nm edge length were prepared by a seed-mediated synthesis and purified before shell growth. In the absence of surface modifiers, hydroxylamine-mediated reduction of $CuCl_2$ produced a conformal Cu_2O shell of 20 nm thickness (**Figure 1a**). Such conformal overgrowth is consistent with our earlier studies of photocatalytically active Au/Cu_2O core/shell nanoparticles.[3] Region-selective Cu_2O shell growth was achieved by pre-incubating nanoprisms with 5-amino-2-mercaptobenzimidazole (AMBI). Sub-monolayer adsorption at 60 °C for 2 h strongly altered the shell nucleation pathway: spectroscopic monitoring of the localised plasmon resonance change revealed a reduced and slower shell deposition, while transmission electron microscopy (TEM) demonstrated Cu_2O domain growth primarily on prism faces and edges and the bare tips were preserved during the process (**Figure 1b**). At moderate AMBI coverage (1 µM, 24% of a monolayer), this tip-exposed morphology was reproducible. At high concentration (>10 µM), however, no shell growth is observed and homogeneous nucleation of free Cu_2O cubes takes place.

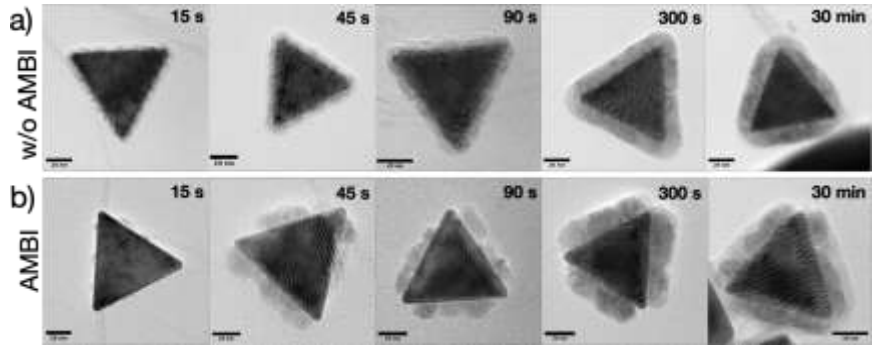

Figure 1. TEM images obtained at different time instances of the Cu_2O shell growth process for the reference (without AMBI) (a) and the AMBI surface-modified nanoprisms (b). Scale bars: 20 nm.

To better understand the impact of surface modification on the development of the tip-exposed nanostructures, we investigated individual nanoparticles before the Cu_2O shell growth using peak-force atomic force microscopy. The experiments confirmed the presence of patchy adhesion domains, that can be attributed to the inhomogeneous distribution of AMBI molecules at the surface, that leads to locally inhibited nucleation.[2] When no AMBI was applied (**Figure 2a**), or AMBI was present in higher-than-optimum concentration (**Figure 2c**), a homogeneously low or high adhesion map was obtained. Hence, the surface-distribution of AMBI is directly related to the Cu_2O shell nucleation and growth at the nanoprisms' surface. The tip-exposed Au/Cu_2O nanoprisms obtained with optimal AMBI concentration preserve both the functional metal–semiconductor interface and the accessibility of the high-intensity plasmonic near-field at the tips. This combination is highly attractive for photocatalytic and optoelectronic applications, where both efficient charge transfer and strong field localization are essential.

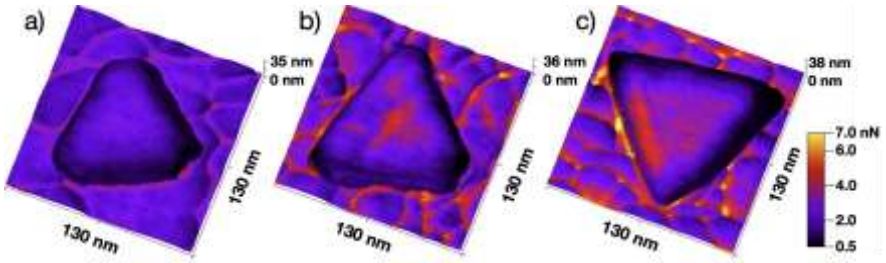

Figure 2. Scanning probe microscopy measurements of the nanoprisms, the color-coded adhesion force map overlain with the topography: no AMBI treatment (a) and surface modification at 1 μM (b) and 190.5 μM AMBI (c).

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HYDROTHERMAL CARBONIZATION OF SPENT COFFEE GROUNDS INTO HYDROCHAR FOR ADSORPTIVE REMOVAL OF RHODAMINE 6G

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Background: Synthetic dyes are persistent pollutants due to their toxicity, stability, and resistance to biodegradation. Rhodamine 6G (Rh 6G), a widely used cationic dye, poses environmental risks through persistence and bioaccumulation [1]. While activated carbon is effective for dye removal, its production often relies on fossil-based feedstocks [2]. Spent coffee grounds (SCG), produced in large quantities worldwide, offer a sustainable and low-cost alternative for adsorbent preparation.

Methods: Hydrochars (HC) were prepared from SCG by hydrothermal carbonization at 160-200 °C for 3-7 h, followed by KOH activation. Materials were characterized by SEM-EDX, FTIR, XRD, TG/DTA, and BET analysis. Adsorption experiments assessed the influence of pH, contact time, adsorbent dosage, and temperature. Kinetics were modeled using pseudo-first-order, pseudo-second-order, Elovich, and Boyd equations, while equilibrium data were fitted with Langmuir, Freundlich, Temkin, and Redlich-Peterson isotherms. Thermodynamic parameters were calculated to evaluate adsorption spontaneity and energetics.

Results: Hydrochar yield decreased with increasing carbonization temperature and residence time, while carbon content and porosity improved. Surface functional groups included hydroxyl, carbonyl, and aromatic groups. Although surface areas were relatively low (2-4 m^2/g), adsorption was efficient, emphasizing the role of surface chemistry. Dye uptake was rapid within the first hour, reaching equilibrium within 3 h. The pseudo-second-order model best described adsorption ($R^2 > 0.98$), indicating chemisorption. At 25 °C, Freundlich fitting suggested multilayer adsorption, while Langmuir dominated at elevated temperatures, pointing to monolayer adsorption. Adsorption was spontaneous ($\Delta G° < 0$) and endothermic ($\Delta H° = 29$-50 kJ/mol). Performance was strongly pH-dependent: negligible uptake occurred at acidic pH, but adsorption increased to ~123 mg/g at pH 10 due to enhanced electrostatic attraction. Increasing adsorbent dosage improved dye removal efficiency (up to 93%) [3].

Conclusion: SCG-derived hydrochars are effective and sustainable adsorbents for Rhodamine 6G removal, combining high performance with low-cost biomass utilization. These findings provide a foundation for developing advanced hydrochar-ZnO composites that integrate adsorption with photocatalysis for wastewater treatment.

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Effect of the reaction conditions on the optical properties of Mn-doped spinel nanostructures

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Zinc gallate ($ZnGa_2O_4$) is one of the promising materials of the AB_2O_4 oxide spinel group that has grabbed the attention of researchers nowadays. This material has wide applications not just because of its general properties such as thermo- and chemical stability and small sizes that characterize the as-prepared nanocrystals, but due to their high band gap (4.4-5.2 eV) and the possibility of several dopants insertion. We can select the dopants in order to get the required material for the application we need. For instance, by varying the dopants we can reach luminescent materials with different emission wavelengths.

The Mn(II) ion-doped zinc gallate (ZGO:Mn or ZGM) nanocrystals have strong green luminescence with an emission around 500 nm, which leads us to a marker nanoprobe, anti-counterfeiting material, or an activator in the field of anticancer therapy[1,2]. The insertion of the Mn(II)-ions is different than the Cr-doping, because in this case the emitters are taking place of the tetrahedral sites of the Zn atoms. This material is synthesized by different methods, such as the sol-gel process, hydro-solvothermal, and solid-state synthesis.

In our research work, we demonstrate the importance of the ratio of the Zn and Ga elements that build up the structures of the host molecule in the reactant mixture, and show the differences in the (magneto) optical properties between the samples with different Za/Ga ratios we had used during the hydrothermal synthesis. Our goal was to find the answer to the question: whether the Mn(II)-doping has the optimal Zn/Ga ratio below the stoichiometric, as the Zn excess helps to reach stronger emission for the Cr-doped zinc gallates.

We analyzed the general properties of the materials with XRD, SEM, and Raman spectroscopy, and studied the optical properties (XEOL, PL, EPR) of the nanustructures synthesized and heat-treated under various conditions. We show that both the reaction conditions and post-annealing have a significant impact on the morphology and the optical properties of the nanoparticles.

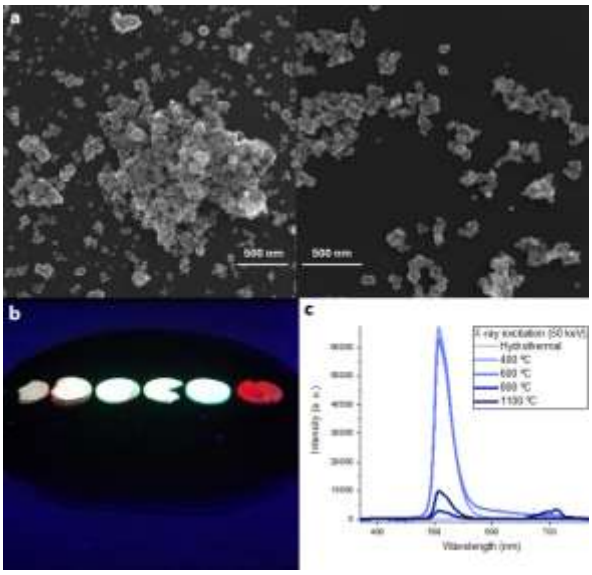

Figure 1. (a) SEM images of ZGM nanoparticles with adjusted Zn/Ga ratio 0.6/2 (left) and 1/2 (right). Notice the diference in morphology. (b) The image shows the luminescence color variation atchieved by adjusting the raction conditions. (c) XEOL spectra of the as-prepared and post-annealed stoichiometric samples.

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ADDITION REACTIONS OF PHOSPHORUS-CENTERED RADICALS ONTO OLEFINS: DFT AND AB INITO CALCULATIONS

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Radicals are reactive species with unpaired electrons. They play important roles in chemistry, biology and even in physics. They are highly reactive, and they are frequently used in industry e.g. to initiate chemical reactions including additions and polymerizations. This computational study aims to explore the addition reactions of phosphorus-centered radicals to functionalized C=C double bonds. Our computational tools allow us to systematically vary both the radical substituents and the olefin functional groups, helping us discover how electronic effects influence reactivity and selectivity. First of all, we introduced the simplest P-centered radicals, including phosphinyl, phosphonyl, and thiophosphonyl species and studied their structures, and their reactions with ethylene. These serve as fundamental models for understanding intrinsic radical behavior without additional stabilization. In order to capture a wider range of stabilization mechanisms and to identify potentially industrially relevant species, we expanded our study to various functional groups, including basic organic substituents, carbonized substituents relevant to industrial photoinitiators such as BAPO-type species, cyclic substituents. The effect of electron-donating, electron-withdrawing groups was revealed. We developed a computational framework to efficiently predict the reactivity of the studied radicals and to design new efficient radicals. We demonstrated that radical stabilization energy (RSE), a descriptor that can be readily obtained from quantum chemical calculations, is directly linked to reactivity, and can serve as a practical predictor for the addition reactivity of phosphorus-centered radicals, especially for σ-type species commonly used in photopolymerization. After evaluating a wide range of phosphorus-centered radicals with ethylene, the study investigates how substituents on olefins affect radical addition reactions. Seven representative P-centered radicals were reacted with 12 different alkenes, to yield geminal (α-attack) or vicinal (β-attack) adducts. The attack at the β-position to yield vicinal adducts turned out to be more favorable both kinetically and thermodynamically. The electronic properties of the substituents strongly influence the reaction. For vicinal adducts, the properties of the substituents on the olefin fragment have a decisive effect on the delocalization of the unpaired electron in the product. π-acceptor groups (e.g., CN, COOMe, NO_2, Ph) enable effective delocalization, resulting in lower spin populations at the α-carbon, and greater thermodynamic stability.

SYNTHESIS, EVALUATION AND CONCENTRATION EFFECTS OF A NOVEL NATURAL-BASED PHOSPHINE ANTIOXIDANT IN THE THERMAL STABILIZATION OF POLYETHYLENE

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A new phosphine-type potential secondary stabilizer was synthesized successfully with large natural raw material content (Fig 1.). The stabilizer is a waxy white powder with a relatively low melting temperature. Both the thermal and storage stability of the stabilizer are sufficient for practical use [1].

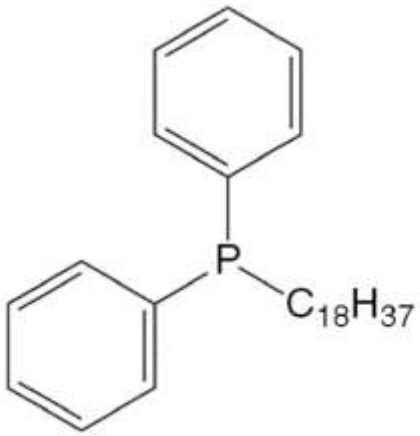

Figure 1. Chemical structure of the new phosphine type secondary stabilizer (NatPhos) [1].

In our work, we used I1010 as a primary antioxidant and the phosphine-type stabilizer as a secondary stabilizer. The aim of our work was to investigate the new phosphine-type stabilizer during multiple extrusions of high density polyethylene (HDPE). We aimed to compare the efficiency as secondary stabilizer with the commonly used stabilizers in the industry (PEPQ and I168) and to determine the optimal phosphine content added from 50ppm to 1000ppm. The optimum was determined by FTIR, melt flow index, oxidation induction time, and colour measurements on extruded samples.

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SUBCRITICAL HYDROLYSIS: A ROUTE FROM WASTE TO RAW MATERIAL

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The growing amount of composite waste—especially from the renewable energy and construction sectors—calls for the development of efficient recycling methods aligned with EU climate goals. This work explores hydrothermal decomposition as a sustainable approach for treating thermoset matrix composites, focusing on two large quantity composite wastes: glass wool insulation waste and decommissioned wind turbine blades.[1-2]

Hydrothermal treatment offers a green chemical recycling route by enabling bond cleavage in crosslinked polymers without toxic reagents.[3] Water acts as hydrolytic reagent, catalyst and solvent at the same time, while elevated temperatures below the critical temperature ensure fast ionic reactions. Pressure is applied to keep the water in a liquid phase.

Different sourced residential glass wool samples were contacted with high temperature and high pressure water in a flow-through setup Under appropriate conditions (250–300 °C), the binder resin decomposed and the products solubilized, while majority of the glass fiber content was preserved. However, slight dissolution of glass was also observed. The reaction was monitored by measuring the pH of the liquid product. The composition of the liquid phase was analyzed by GC–MS, revealing decomposition products originating from a phenolic or bisphenol A-type resin. Meanwhile, the specific surface area of the recovered fibers increased, reaching 101.5 m^2/g, creating the possibility for application as catalyst carriers or in other fields requiring high specific surface area. Alternatively, the purified glass may be remolten.[4]

The same methodology was extended to a decommissioned wind turbine blade composite obtained from Anmet Co., Poland. The blade composite fraction was mainly based on bisphenol A epoxy resin and glass fibres. Following the method optimization on a model resin optimal condition: 360 °C and 25 MPa, complete conversion in 10 minutes, selective product profile consisting mainly of phenol, bisphenol A, and 4-isopropenylphenol), the method was applied to the wind blade samples with comparable efficiency. Clean glass fibers were recovered, as confirmed by scanning electron microscopy and thermogravimetric analysis, showing >99% purity and no visible damage.

This combined approach in a scalable flow-through setup demonstrates the versatility of subcritical water treatment for complex composite waste. The ability to recover high-purity glass fibers and identify useful organics in the liquid phase supports not only landfill diversion but also the valorization of waste streams in line with circular economy principles.

Funding Sources

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Reconciling Economic Growth and Sustainability: Is a Balance Possible?

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The transition from fossil fuels to renewable energy is a global imperative to mitigate climate change and environmental degradation. However, policy and scientific discourse often overlook the systemic trade-offs involved in such a transformation. In our study[1], a novel framework was introduced: the Sustainable Worldwide Energy Transition (SWET) model, designed to quantify these trade-offs under a wide range of economic growth and energy transition scenarios. Unlike conventional approaches, SWET integrates the energy costs of ecosystem maintenance, renewable infrastructure deployment, and carbon dioxide removal, thereby providing a more realistic picture of the net energy available to society.

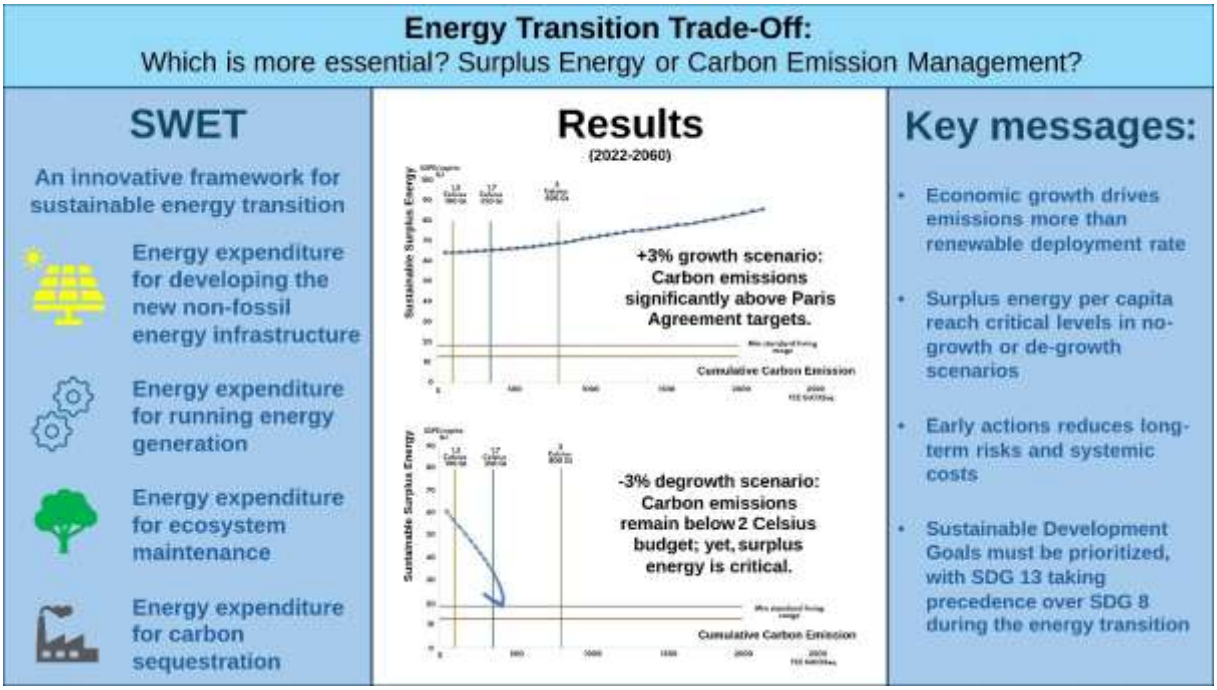

Figure 1. Graphical abstract of the SWET model.

The analysis combined three International Energy Agency (IEA) transition pathways—Stated Energy Policies (STEPS), Announced Pledges (APS), and Net Zero by 2050 (NZE)—with seven global GDP growth trajectories ranging from −3% to +3% per year. This yielded 21 scenarios, allowing for a comprehensive exploration of the interplay between economic throughput, carbon emissions, and energy sufficiency.

Results demonstrate that continuous positive economic growth is fundamentally incompatible with the Paris Agreement climate goals. In high-growth scenarios (+3% GDP), cumulative carbon emissions exceed 2000 $GtCO_{2eq}$ by 2060, far surpassing the 2°C carbon budget. Conversely, degrowth scenarios can achieve compliance with carbon limits, but at the expense of a sharp decline in net societal energy availability. In the most extreme case (−3% GDP), the Sustainable Surplus Energy (SSPE) per capita—the energy remaining after accounting for all

system costs—falls to 15–25 GJ/year/capita, which approaches the minimum thresholds for decent living standards.

The findings highlight a paradox: while accelerated renewable deployment is essential, it is insufficient if pursued within a paradigm of perpetual economic growth. Technological optimism alone cannot resolve the structural contradictions between rising economic output, limited carbon budgets, and declining energy returns on investment (EROI). Instead, the SWET model suggests that managed economic contraction and a reordering of policy priorities are unavoidable if societies are to maintain both climate safety and social viability.

A central innovation of SWET is the operationalization of sustainable surplus energy as a new systems-level metric. SSPE accounts for the true costs of building, maintaining, and compensating the externalities of energy systems, thus moving beyond simplistic measures of gross energy supply. This metric offers policymakers a robust tool to evaluate the feasibility of transition pathways under real-world constraints.

In conclusion, the study provides quantitative evidence that the trade-offs of the global energy transition extend far beyond technological deployment rates. The results indicate that it is not possible to simultaneously achieve climate stabilization, ensure sufficient surplus energy for all, and sustain global economic growth. Addressing this triple challenge requires a fundamental rethinking of sustainability narratives and development goals. The unavoidable sacrifices revealed by the SWET model must be acknowledged to design credible policies for a just and effective energy transition.

The talk not only showcases the results of the SWET model but also addresses the challenges of worldwide decoupling. Separating economic growth from the consumption of materials and energy has always been a component of sustainable development objectives. Some theories suggest that technical developments could enable economic growth while minimizing environmental effect. Nevertheless, the notion has yet to be substantiated in practice, and it can be demonstrated through the principles of thermodynamics that absolute decoupling – defined as a total reduction in environmental effect concurrent with economic growth – is an unattainable global objective.

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Quantification of amorphous traces in crystalline carvedilol using different analytical methods

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Many active pharmaceutical ingredients (APIs) are marketed in crystalline form, and most APIs under development also exhibit crystalline forms. However, during the downstream processing of crystalline APIs, a small degree of amorphization can occur, particularly during steps involving high pressure, friction, or rising temperature (e.g. micronization)[1,2]. Such partial amorphization can alter e.g. the moisture sensitivity, the dissolution properties, and the bioavailability; therefore, investigation of amorphous traces is a crucial quality assurance question. As the detection of low amount amorphous form in a crystalline material is challenging, development of reliable analytical methods to quantify amorphous traces became an important task of the pharmaceutical industry[3].

In this study, amorphous carvedilol was produced by quench cooling and milled to powder form. Polarized light microscopy, X-ray powder diffraction and differential scanning calorimetry were used to verify the success of amorphization. Calibration samples containing defined mixtures of amorphous and crystalline material were analyzed using thermally stimulated depolarization current (TSDC) analysis and Raman spectroscopy. Calibration curves were constructed for both techniques, and additional mixtures were prepared to validate the calibration methods.

Both TSDC and Raman spectroscopy demonstrated sufficient sensitivity to quantify low levels of amorphous content in crystalline matrices. Besides, the Raman spectroscopy-based analysis required no sample preparation and was performed non-destructively, while TSDC analysis needed shorter measurement time. These advantages are highlighting the potential of these methods for routine quality control in this field.

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Impact of Genomic Uracil on Zebrafish Embryonic Development

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Uracil is a fundamental building block of RNA as a ribonucleotide base, but it can also appear in DNA as deoxyuridine. Uracil can be incorporated into DNA via two pathways: enzymatic or spontaneous oxidative deamination of cytosine basis, which is mutagenic, and the misincorporation of dUTP instead of dTTP when the cellular dUTP:dTTP ratio is imbalanced [1]. Even though the second incorporation mechanism is not mutagenic, the presence of uracil in the genome is recognised as mutagenic and requires prompt repair. Uracil-DNA glycosylase (UNG) is the main repair enzyme that maintains low genomic uracil levels. Additionally, dUTPase plays a critical role by catalysing the hydrolysis of dUTP to dUMP, thereby reducing the cellular dUTP:dTTP ratio and simultaneously supplying dUMP as a substrate for *de novo* thymidylate biosynthesis [2].

Our previous findings in *Drosophila melanogaster* revealed that genomic uracil levels are elevated during the third larval stage of development and that corresponding metabolic enzymes are critical for successful development [3]. Building on this work, we extended our investigation to the early stages of embryonic development using zebrafish (*Danio rerio*), a vertebrate model system well-suited for molecular studies of early development [4]. We isolated genomic DNA from distinct embryonic stages and quantified the uracil content by the dot blot method [1]. Strikingly, we observed a significant accumulation of genomic uracil preceding the maternal to zygotic transition (MZT), a critical developmental phase characterised by the onset of zygotic genome transcription, active clearance of maternal mRNAs, and the transfer of developmental control to the zygote [5]. The high genomic uracil levels were accompanied by high dUTP levels in the dNTP pools. To investigate the underlying causes of these elevated levels, we measured the mRNA expression of genes involved in uracil metabolism. We also performed microinjection experiments by microinjecting active and inactive forms of the dUTPase enzyme into fertilised oocytes. The active enzyme significantly reduced the dUTP levels within the first hour post-fertilisation compared to the inactive enzyme and proved to be either lethal or caused morphological changes, whereas the inactive enzyme had no such effects. To explore whether genomic uracil incorporation follows a specific pattern, we conducted U-DNA sequencing using our previously developed U-seq method [6]. We found that genomic uracil patterns preceding the MZT significantly associate with genomic markers critically involved in transcription activation.

These results show that the genomic uracil plays an important role in the early stages of embryonic development. Based on sequencing, we hypothesise that this high genomic uracil is involved in MZT by activating genomic transcription.

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RESVERATROL'S EFFECT ON A MAB PRODUCING CHO CELL LINE

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One of the most important issues in industrial production is how much yield can be achieved. For optimalization the number of living cells can be increased, the conditions such as aeration can be changed, or chemically defined additives can be added.

CHO (Chinese hamster ovary) cells have long been used in industrial production to produce human recombinant proteins. Being mammalian cells, they produce glycosylated proteins, in addition, they create post-translational modifications very similar to those of humans. This is why they are suitable for creating monoclonal antibodies, which can be used for analytical or therapeutic purposes[1].

Most people have probably heard of resveratrol thanks to red wine. As an antioxidant molecule, it can neutralize free radicals, thus it is generally protecting against oxidative stress. This is important in itself, since the reactive oxygen derivatives formed can cause the loss of function of protein molecules, the formation of lipid peroxides, or even cell death[2]. In a reactor, cells are exposed to many stressors, and if we can mitigate their effects, it can lead to increased productivity.

However, resveratrol also has another known property, its ability to arrest the cell cycle[3]. If we can use this trait, then cells may spend more of their energy on protein production.

The main direction of our studies was decided by these two properties and the idea that through them we may be able to achieve a significant increase in yield.

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Abstracts of students' poster presentations

COMPARISON OF METHODOLOGIES FOR COLOUR MEASUREMENT IN FRESH CHICKEN BREAST FILLETS UNDER DIFFERENT STORAGE TEMPERATURES

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Colour is one of the most important quality indicators of fresh poultry meat, exerting a substantial influence on consumer acceptance and serving as a marker of freshness and stability during storage. Accordingly, dependable methods for the instrumental measurement of colour are essential when assessing the impacts of storage temperature and duration on meat quality [1].

This study compares two methodological approaches to colour measurement in fresh chicken breast fillets stored under constant and fluctuating temperature regimes over 5 days. In the initial method, pre-packaged sets of three fillets were repeatedly measured through intact vacuum packaging. Calibration and measurement were performed within the packaging, and samples were returned to storage after each daily measurement. This approach facilitated the assessment of colour stability when measuring the same fillets over time. In the subsequent method, vacuum-packaged fillets were opened daily and measured individually, with calibration conducted against household plastic wrap placed over the fillet surface, thereby simulating real-world product acceptance where different fillets are received each day.

The study compares two approaches, highlighting differences in colour parameter stability (L*, a*, b*), measurement repeatability, and practical application in long-term storage investigations. These findings aid in selecting suitable methods for colour evaluation in poultry research, thereby ensuring reliable quality assessment and promoting waste reduction in line with sustainability objectives. The study demonstrates that instrumental colour measurement is a valuable tool for quality assessment at the point of product acceptance. Routine measurement of fresh fillets provides useful insights into freshness and contributes to quality control within the poultry industry and retail sector.

Keywords: chicken breast, colour measurement, quality control, storage temperature, freshness

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IDENTIFICATION OF CLIMATE CHANGE PREDICTIVE PARAMETERS IN HUNGARIAN ACACIA HONEYS

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Climate change poses significant challenges to beekeeping, as variations in temperature and precipitation directly affect plant flowering, nectar production, and consequently honey yield and composition[1]. Honey, as a natural product, offers an opportunity to monitor ecological processes through its pollen spectrum, phenolic compounds, mineral content, and moisture content[2,3,4]. The aim of this study was to identify climate-sensitive parameters and evaluate their predictive potential in Hungarian acacia honey. Samples were collected over four years from ten counties with different climatic and topographical conditions. Moisture content, selected phenolic compounds (4-hydroxybenzoic acid, caffeic acid, p-coumaric acid, ferulic acid, coniferaldehyde, chrysin), pollen composition, and the concentrations of calcium, potassium, magnesium, and phosphorus were determined. Meteorological variables, including temperature and precipitation, were also studied.

Strong correlations were observed between climate variables and several honey constituents: the proportion of Robinia pseudoacacia pollen was depended on temperature, while phenolic compounds such as 4-hydroxybenzoic acid and caffeic acid showed a positive correlation, and ferulic acid showed a negative correlation with precipitation. Mineral content showed marked regional variation: in less diversified, agriculture-focused counties (e.g., Jász-Nagykun-Szolnok, Nógrád, Fejér), predominantly negative correlations with temperature were identified, whereas in more ecologically diverse and fruit-producing regions (e.g., Szabolcs-Szatmár-Bereg, Tolna, and partly Hajdú-Bihar and Pest), positive correlations were more common, suggesting that diversified vegetation may mitigate adverse climatic impacts [5,6,7].

In economically disadvantaged counties (particularly Nógrád and Hajdú-Bihar) beekeepers often lack the financial resources necessary to adapt, which increases their vulnerability to climate change. These results highlight the importance of taking ecological and social-economical aspects as well as climatic effects into account in beekeeping, as these effects are reflected in the composition and thus the quality of honey. Such knowledge can provide valuable support for the development of proactive adaptation strategies, helping beekeepers mitigate the adverse effects of climate change.

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Development of nanocellulose-based carriers for immobilization and purification of recombinant enzymes

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Biotechnology represents one of the fastest-growing sectors of industry in this century. In numerous sectors, the application of biotechnological methods has become essential, as traditional approaches often do not achieve the necessary standards of product selectivity and purity. In contemporary discussions, the environmental costs associated with industrial processes have become a critical aspect to evaluate [1]. These issues can be mitigated by using enzymatic techniques, which have a high selectivity and can achieve reactions at considerably mild conditions compared to traditional synthetic methods. The main issue of enzymatic processes is the proteins' sensitivity to solvents, pH, and temperatures, which can be improved with enzyme planning, modification, or immobilization [2]. Immobilization enhances enzyme stability and separation from reaction media by attaching them to solid organic or inorganic carriers [3]. Immobilization methods (physical or chemical binding) may influence the enzymatic process, and the proper system can multiply the enzyme's effectiveness severalfold [4]. In the production of enzymes, recombinant methods are getting a lot more prevalent due to their higher productivity, scalability, and modifiability [5-6]. The produced enzymes must also be purified, so-called tags for affinity chromatography are really popular. [7]. In the case of His-tag, the main method is using agarose-based Ni-NTA resins. These are highly efficient, but if improperly stored, they can become biologically contaminated, and if they dry out, the resin beads' structure can collapse.

The goal of our work is the production of a bacterial nanocellulose-based carrier system, which can bind His-tag-labeled proteins reversibly and is useable in the purification of these proteins instead of the conventional agarose-based Ni-NTA resins. The main purpose of the work is to improve the stability and efficiency of the carriers compared to the commercial resin.

To achieve our goal, bacterial nanocellulose membranes were produced by applying food-grade bacterial nanocellulose (NC) "nata de coco." NC membranes (NCM) were chemically functionalized to ensure specific binding groups loaded with metal ions to bind the His-tag enzyme. The effect of different metal ions, nickel(II), cobalt(II), and iron(III), and chemical functionalization methods on the binding properties of NC membranes was investigated. The protein binding experiments were carried out with *Anabaena variabilis* phenylalanine ammonia lyase (AvPAL) as the model enzyme. The study also examined the enzymatic activity of both recycled and immobilized *Av*PAL on NCM.

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CONTINUOUS TWIN-SCREW WET GRANULATION USING POTASSIUM SODIUM TARTRATE TETRAHYDRATE

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Prior to tableting, active pharmaceutical ingredients (APIs) and excipients with inadequate flow and compressibility properties are granulated to improve their tabletability. The most common type of granulation is wet granulation, in which granulation liquid is added to bind the particles together. Granulation is one of the main areas of pharmaceutical research and development as it is a key step in the development of solid dosage forms. At the same time, the development of continuous, integrated production lines from powder to tablets is also underway.

During the present research, a new wet granulation technology was investigated on a fully continuous, integrated production line in terms of operation and scalability. The continuous system included a feeding, granulation, cooling, milling, and tableting step. The new wet granulation technique does not require the addition of granulation liquid to the starting powder mixture, so only minimal cooling is required after granulation, resulting in a more energy-efficient process for the pharmaceutical industry. This is achieved by adding an excipient, potassium sodium tartrate tetrahydrate (PST), to the powder mixture. PST has a high crystal water content, which is released when heated, resulting in an in-situ granulation liquid during the process. Using this wet granulation-based technology, granules with excellent flow properties were produced and immediate-release tablets with less than 1% friability, requiring a force of more than 100 N to break and a tensile strength of 1.5 MPa were compressed. Continuous production allowed for a simple scale-up from 0.5 to 10 kg/h using the same equipment. In summary, the method studied may be a promising technology for the pharmaceutical industry.

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Carbopol ® and hydroxypropyl methylcellulose films for mucoadhesive drug delivery system

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Oral drug delivery continues to be the most favored method of administration owing to its ease and patient compliance. Conventional dosage formulations frequently provide insufficient bioavailability, degradation in the hostile gastrointestinal environment, and restricted residence time at the absorption site. Mucoadhesive polymeric films have surfaced as a viable solution to address these problems, facilitating targeted administration, avoiding the first-pass metabolism, and enhancing therapeutic efficacy [1,2,].

The efficacy of drug delivery systems is significantly influenced by the physicochemical and mechanical characteristics of their excipient materials. Polymeric films intended for mucoadhesion must demonstrate appropriate rheological properties, water absorption, tensile strength, and adherence to biological tissues, while ensuring drug stability and controlled release. By customising these material properties, one can improve the reliability and efficiency of mucoadhesive drug delivery systems [2,3,4,5].

I aimed to study the possible application of hydroxypropyl methylcellulose (HPMC) and Carbopol® films for mucoadhesive drug delivery systems owing to the unique functional characteristics of these polymer excipients. I utilised poly (vinyl alcohol) (PVA) hydrogels as biomimetic mucosal substrates to mitigate the limits of biological tissue variability in adhesion measurements. PVA gels, owing to their adjustable water content, mechanical compliance, and hydrophilic nature, offer a consistent platform that closely mimics the viscoelastic and adhesive properties of natural mucosa [1,2]

Two percent (w/w) solutions of HPMC and Carbopol® were prepared in water for 24 hours, resulting in translucent HPMC and opaque Carbopol® dispersions. Films were cast from polymer solutions of varying thicknesses to PVC foils and subsequently dried at room temperature. Oscillatory rheology measurements were assessed on both dry and pre-swollen films, the latter achieved by adding a drop of water to the surface of the films followed by its swelling for 20 minutes to simulate hydration during contact with tissues. The films were analysed for their thickness, mechanical characteristics, swelling capacity, and adhesion strength to mucosa-mimetic PVA hydrogels.

Oscillatory rheology demonstrated a decrease in the storage modulus (G′) upon hydration, indicating that the polymer is still viscoelastic with enhanced chain mobility, which is important for mucoadhesion. Film thickness of 400-600 µm resulted in maximum elasticity, hydration, and structural integrity, while thinner films disintegrated more easily after 20 min of swelling, whereas the swelling of thicker films was inhomogeneous.

The research indicated that the adhesion force and work of adhesion of Carbopol and HPMC films can be affected by film thickness. For both polymers, an increase in film thickness typically led to an enhanced adhesion force, indicating improved interfacial contact with the substrate.

Notwithstanding substantial advancements in mucoadhesive formulation creation, heterogeneity in adhesion efficacy persists as a key problem, affected by both biological and formulation-related variables. Currently used polymeric films frequently exhibit diminished adherence and variable drug release, constraining their applicability in therapeutic settings. This study can contribute to the design of innovative polymeric systems that include poly (aspartic acid) derivatives into HPMC and Carbopol® based films to improve mucoadhesive efficacy and controlled drug release.

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PHASE EQUILIBRIUM AND DENSITY MEASUREMENTS FOR THE SYSTEM METHYL ACETATE + SUNFLOWER OIL + CARBON DIOXIDE

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Supercritical fluid processes attracted significant attention as alternatives to conventional techniques in different fields like fractionation, cleaning and material processing, extraction, and micronization. It is also considered to be a good alternative in reaction mediums, as opposed to organic solvents, for conducting enzymatic reactions[1,2]. In this study, we studied the phase equilibrium and density of the system methyl acetate, sunflower oil, and CO_2 because of its importance in the biodiesel production with interesterification reaction, where CO_2 is used here as a cosolvent. To estimate the phase equilibrium of this system, we need the interaction parameters of the binaries (methyl acetate + CO_2, sunflower oil + CO_2, and methyl acetate + sunflower oil). The binary systems (methyl acetate + CO_2, sunflower oil + CO_2) were fitted to experimental and literature data to get the interaction parameters, which are shown in Table 1 by using Aspen Plus software with Peng-Robinson (EoS). The third system (methyl acetate + sunflower oil) is not available in the literature, and it is hard to measure. So, the interaction parameters of this system, which are shown in Table 1, were estimated based on the experimental data of the ternary system at different operational conditions using the view cell. The used conditions were temperature (35-85 ºC), molar ratio of methyl acetate to sunflower oil (9, 15, and 30), and CO_2 weight fraction based on the mixture (0,2-0,4). The interaction parameters in Table 1 were used to estimate the phase equilibrium of the ternary system, which is shown in Figs. (1-3) using Aspen Plus software. Using Peng-Robinson to estimate the phase equilibrium showed very good results, but the density results were not accurate. The density results were fitted to the Tait equation using MATLAB software to get more accurate results[3]. The parameters of the Tait equation were predicted based on the experimental measurements at different conditions using the view cell as well. These parameters were used to predict the density data, like Fig. 4.

Table 1: Interaction parameters for the binary systems.

Binary system	k_{ij}	k_{ji}	l_{ij}	l_{ji}	Basis of regression
CO_2-Methyl acetate	-0,018811561	-0,018809399	0,026561407	0,117355391	This work and Ohgaki
CO_2-sunflower oil	0,015287726	0,015276261	-2,64356536	-0,032483977	This work
Methyl acetate-sunflower oil	0,074052985	-0,772001209	8,18486186	-0,641177356	This work basing on the ternary system results

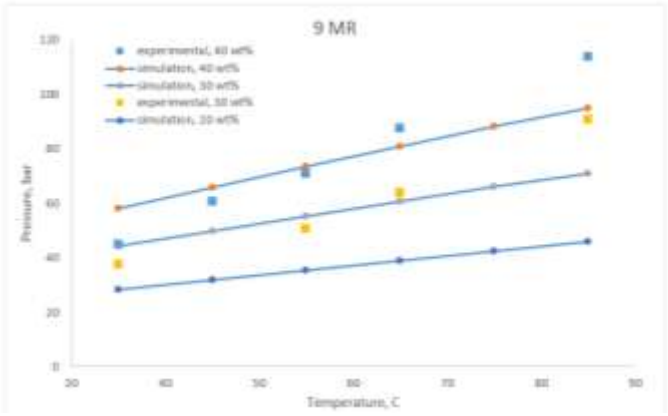

Fig.1: Experimental and Simulation results for methyl acetate + sunflower oil + carbon dioxide phase equilibrium at MR=9.

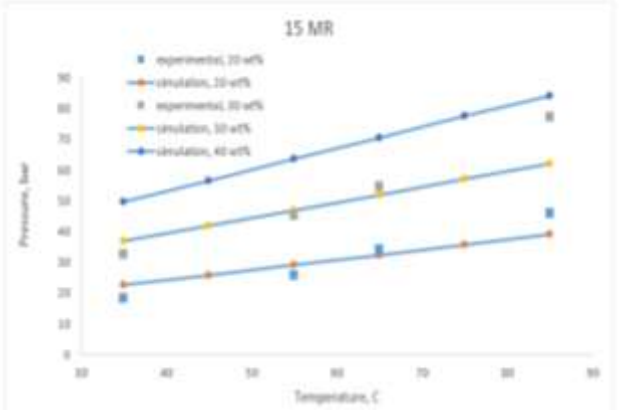

Fig.2: Experimental and Simulation results for methyl acetate + sunflower oil + carbon dioxide phase equilibrium at MR=15.

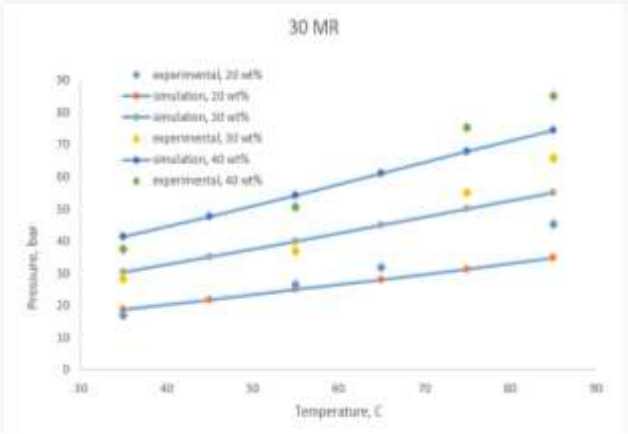

Fig.3: Experimental and Simulation results for methyl acetate + sunflower oil + carbon dioxide phase equilibrium at MR=30.

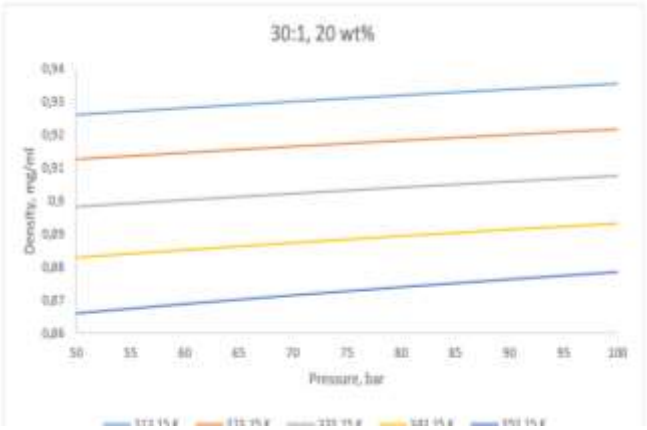

Fig 4: Estimated density for methyl acetate + sunflower oil + CO_2 ternary system at MR=30, CO_2 wt%= 20%.

Acknowledgments

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THIADIAZINO-INDOLE, THIADIAZINO-CARBAZOLE AND BENZOTHIADIAZINO-CARBAZOLE DIOXIDES: SYNTHESIS, PHYSICOCHEMICAL AND EARLY ADME CHARACTERIZATION OF REPRESENTATIVES OF NEW TRI-, TETRA- AND PENTACYCLIC RING SYSTEMS AND THEIR INTERMEDIATES

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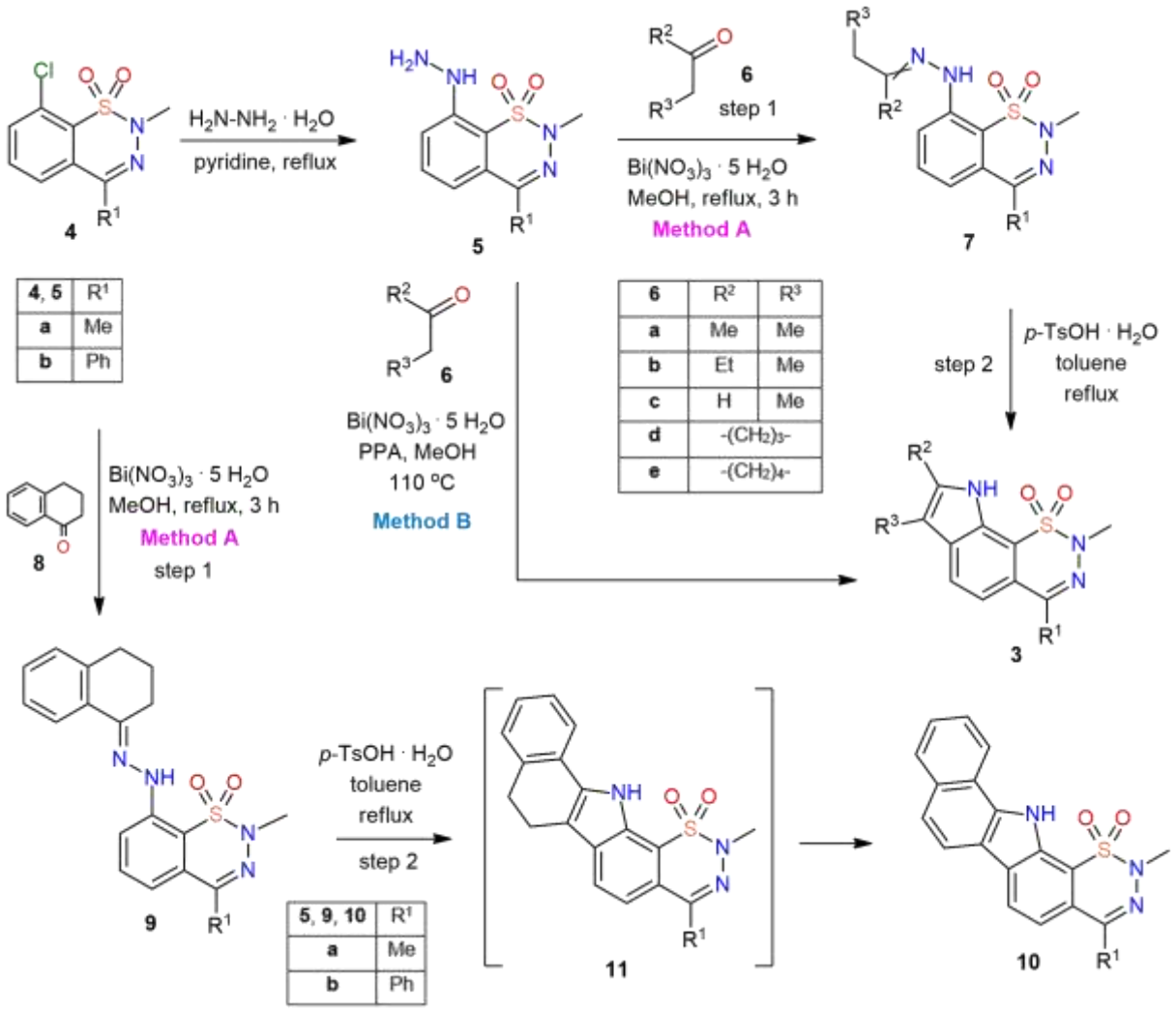
In light of the well-established and broadly indicated pharmacological activity of phthalazin-1(2*H*)-one, we have devoted significant effort to the synthesis and pharmacological investigation of structurally related 1,2,3-benzothiadiazine 1,1-dioxides over the last decade. Motivated by the *in vivo* anxiolytic activity of 1,2,3-benzothiadiazine 1,1-dioxides, we aimed at elaborating a synthetic procedure for the preparation of their pyrrole-fused counterparts, 2,9-dihydro[1,2,3]thiadiazino[5,6-*g*]indole 1,1-dioxide derivatives, as it is well known that synthetic as well as naturally occurring compounds containing an indole moiety exhibit diverse biological activities including psychiatric disorders and neurodegenerative diseases.

We synthesized target compounds **3** exhibiting new tricyclic and tetracyclic ring systems starting from 8-chloro-2,4-dimethyl-2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**4a**) and 8-chloro-2-methyl-4-phenyl-2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**4b**). Treatment of compounds **4a**,**b** with hydrazine monohydrate afforded 8-hydrazino derivatives (**5**) as suitable starting materials for the construction of the indole structural element of compounds **3** by Fischer indole synthesis. Pentacyclic derivatives (**10**) were also prepared in the same two-step way as compounds **3** above, starting also from hydrazines **5a**,**b**, in two steps.



*Scheme 1. Synthesis of tri- and tetra- and pentacyclic thiadiazinoindole dioxides **3** and **10**.*

This simple and versatile process led, via Fischer indole cyclization of the corresponding hydrazones, to a wide structural variety of new tri-, tetra- and pentacyclic ring systems. The structural characterization of (*E*)- and (*Z*)-hydrazones was supported by 2D NMR techniques, while that of the target compounds by single-crystal X-ray measurements. The hydrazone intermediates and the new title compounds were subjected to a physicochemical and early ADME characterization study, in the framework of which log*P*, pK_a and log*k* values were calculated. Following that, kinetic solubility and in vitro gastrointestinal membrane-specific permeability measurements were carried out to assess the lead-likeness of the compounds. Subsequently, the metabolic stability of the most promising derivatives was also determined using human liver microsomes. Based on literature analogy with related compounds, furthermore on calculated properties, and results from kinetic solubility, in vitro membrane permeability and metabolic stability measurements, a tetracyclic derivative, 2,4-dimethyl-2,7,8,9,10,11-hexahydro-[1,2,3]thiadiazino[6,5-*a*]carbazole 1,1-dioxide (**3e**) has been identified as a promising central nervous system drug candidate for pharmacological testing and eventual further structure-activity optimization.

REACTIVE COMPATIBILIZATION OF IMMISCIBLE PLA/PBAT BIOPOLYMER BLENDS FOR MEDICAL APPLICATION

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Introduction: The modulus of the PLA used for medical purposes is large and might damage softer tissues around an implant or scaffold prepared from it.[1] The purpose of combining PLA with PBAT is to reduce stiffness. However, the two polymers are immiscible and only slightly compatible[2], so the compatibility of the two materials must be improved in some way. One possible approach is the chemical coupling of the components by reactive processing.[3]

Experimental: An isocyanate is used as coupling agent to form "in-situ" copolymer and a cobalt-stearate catalyst is also added in some cases to increase the number of end groups of the polymers capable of the coupling reactions. The effect of the amount of coupling isocyanate on compatibility, structure and properties is investigated in this study. PLA (Natureworks Ingeo PLA 4032D) and PBAT (BASF PBAT Ecoflex F Blend C1200) were dried at 60 °C for 24 hours in a vacuum oven before processing. The dried pellets were introduced into a Haake internal mixer with increasing amounts of MDI isocyanate and reacted at 180 °C, 50 rpm for 30 minutes. Mechanical properties (Instron 5566) were determined and DMA (Perkin Elmer Diamond), DSC (Perkin Elmer DSC 7), as well as FTIR-ATR (Bruker Tensor 27) measurements were carried out on 1 mm thick compression molded specimens. Structure was studied by SEM (Jeol JSM 6380 LA). The result of the chemical reactions was investigated with GPC (Agilent Infinity 1260) and NMR (600 MHz Varian NMR spectrometer) measurements.

Results and Discussion: NMR and GPC results prove that the isocyanate is built into the chain. The structure of the blend changes drastically during reactive processing; the rough IPN morphology changes to dispersed structure with varying particle size as a result of reactions. The decreasing size of the dispersed phase indicates improved compatibility. Changing glass transition temperatures show the modification of structure, interactions and compatibility (Figure 1.). Coupling modified properties considerably (Figure 2.). The modulus of the blends changes only slightly, but stiffness is not sensitive to structure and interactions. The addition of the cobalt(II) stearate catalyst does not result in transesterification reactions, but in a decrease of molecular weight.

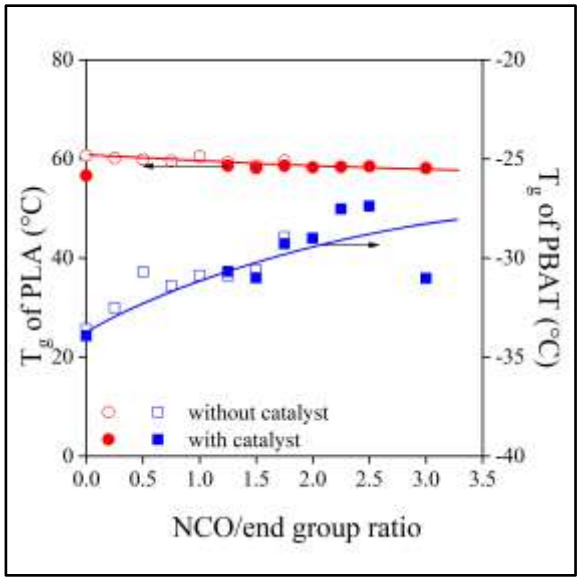

Figure 1. Effect of NCO content on the glass transition temperature of the components.

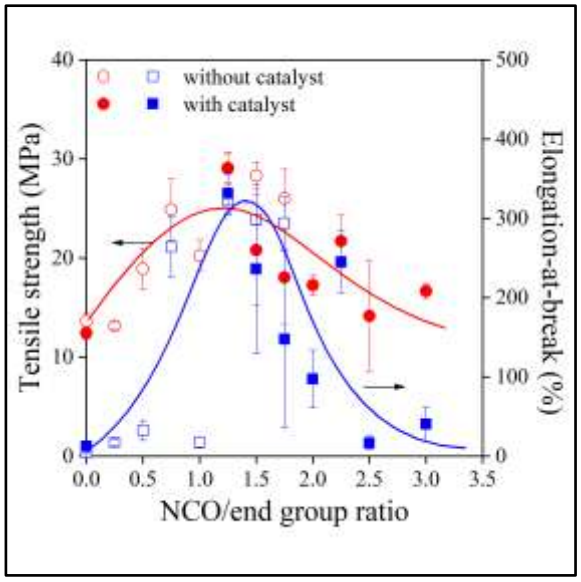

Figure 2. Dependence of the mechanical properties of the blends on NCO content.

Conclusions: Some questions remained open about the mechanical properties of the blends and the effect of the $CoSt_2$ catalyst. The evaluation of structure, properties and compatibility continues. The composition of the reaction mixture, especially $CoSt_2$ content must be optimized in the future.

Acknowledgments: The project supported by the Doctoral Excellence Fellowship Programme (DCEP) is funded by the National Research Development and Innovation Fund of the Ministry of Culture and Innovation and the Budapest University of Technology and Economics. Chinda Thavivanh and László Cseke are acknowledged for their help in sample preparation. Bálint Imre is thanked for IR measurements.

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CHEMICAL RECYCLING OF FLEXIBLE POLYURETHANE FOAMS BY GLYCOLYSIS: TOWARD A MORE SUSTAINABLE POLYOL RECOVERY

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Introduction

Since polyurethanes are among the most versatile polymers, their application has grown significantly in recent years. As a direct result of their commercial success, the generation of PU waste has risen significantly. According to the European Bedding Industry Association, up to 30 million mattresses reach their end of life annually and the most common waste management practice is still landfilling, which is the least preferred measure.

The increasing amount of landfilled waste polyurethane foams (PUFs) and recent EU directives increase the need for effective reuse and recycling end-of-life scenarios for polyurethane foams. Mechanical recycling cannot provide the ultimate solution. Consequently, chemical recycling processes are preferred. The chemical recycling of polyether polyol-based PUFs is based on the cleavage of the urethane bonds, leaving ether groups in the polyether polyol intact. The current methods available are acidolysis, hydrolysis, aminolysis and glycolysis. Our research focuses on the optimization of the glycolysis process which has high potential for commercialization.

Experimental

Industrial waste samples of scrap flexible PU foam were reacted in a 1:3 mass ratio with different glycols, i.e. diethylene glycol (DEG), glycerol (GLY). The catalyst used was potassium acetate (KAc). Reactions were performed at 180–220 °C in a 500 mL glass reactor under an argon atmosphere. Foam was added manually, followed by 3–6 hours of stirring. Products were separated in a separatory funnel, and the phases were analyzed by hydroxyl number determination, rotational viscometry, and FTIR spectroscopy.

Results and Discussion

The glycolysis process usually results in a two-phase product (two liquid layers). The upper layer mainly consists of the recovered polyol. The lower layer contains the excess glycol and other residues from the PUF. The viscometry measurements and FTIR spectroscopy revealed distinct profiles between upper and lower phases. The IR spectra of the upper phases of the repolyols showed strong agreement with that of the virgin polyol, except in the spectral regions associated with hydroxyl (OH) groups, where repolyols exhibited significantly stronger absorption. These IR findings were supported by hydroxyl number determination, which revealed that the repolyol obtained from glycolysis had a substantially higher hydroxyl value than the virgin polyol, indicating a higher content of reactive functional groups.

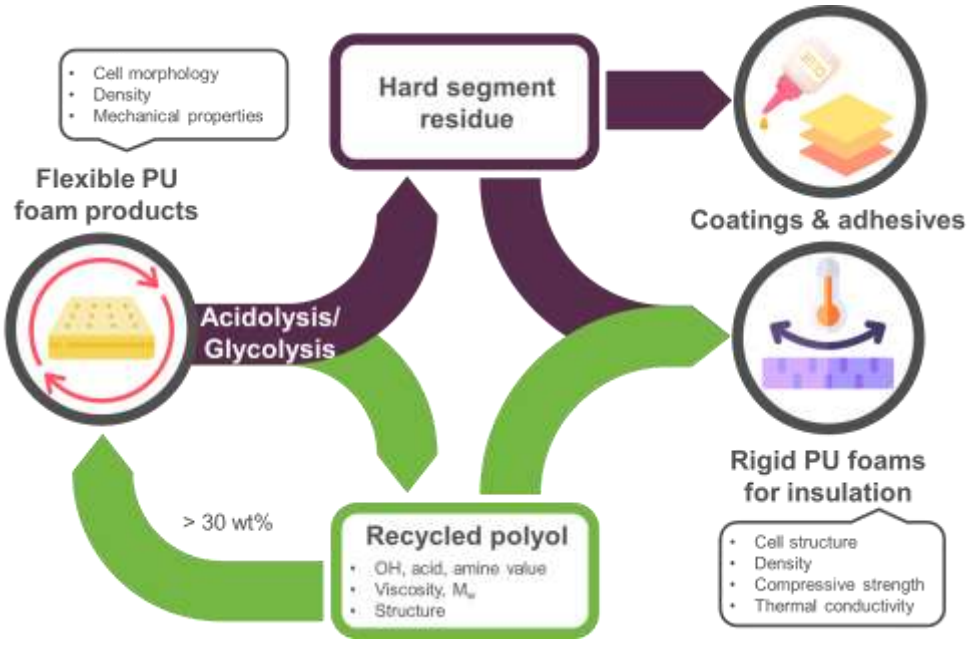

Figure 1. Project concept.

Conclusions

This study demonstrated the feasibility of chemically recycling flexible PUF through glycolysis using various solvents. Among the tested systems, diethylene glycol combined with potassium acetate proved most effective in achieving phase-separated products suitable for further analysis and potential reuse. However, the exploration of greener alternatives, such as the use of glycerol – a by-product of biodiesel industries – represents a promising direction toward more sustainable recycling technologies. The study also revealed significant challenges in process optimization, as multiple variables interact in complex ways to influence the efficiency and outcome of the glycolysis. Continued development, possibly assisted by systematic experimental design, is essential to enable scalable, eco-friendly polyurethane recycling.

Acknowledgments

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CHARACTERIZATION OF MUCOADHESION OF POLYMER TABLETS ON THE SURFACE OF POLY(VINYL-ALCOHOL) HYDROGELS

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An essential pharmaceutical aim is to achieve high bioavailability of the active ingredients in both local and systematic drug administration. Mucoadhesive dosage forms (e.g., mucoadhesive tablets or patches) offer higher bioavailability of the active ingredient via different routes of administration (e.g., ocular, nasal, vaginal and buccal) compared to the conventional pharmaceutical forms. The reason for this is the adherence of mucoadhesive excipients (mainly polymers) onto the mucus membrane, which allows the drug to be absorbed directly through the tissue, bypassing the first-pass metabolism, i.e., avoiding the degrading effects of the stomach or liver [1, 2].

The process of mucoadhesion is complex, thus its understanding and control are not yet complete, which would be essential for the rational development of efficient dosage forms. The evaluation of ex-vivo mucoadhesion tests, performed on animal mucous membranes, is difficult due to the natural diversity of the biological samples. Moreover, use of animal samples brings up many ethical questions, thus mucosa mimetic materials are needed [3]. Hydrogels with high water content and reproducible structure could be ideal mucosa mimetic materials, since their viscoelastic and adhesion properties can model properly the properties of the natural mucous membranes. Therefore, measurements performed on hydrogels can significantly contribute to the understanding of subprocesses of mucoadhesion [3, 4].

Synthetic poly(vinyl alcohol) (PVA) and mucin – the main macromolecular component of mucus [5, 6] – containing PVA (muc/PVA) mucosa-mimetic hydrogels were developed by the Soft Matters Group for the reproducible modelling of mucoadhesion [7, 8]. Our results indicated that PVA and muc/PVA hydrogels are promising mucosa mimetic materials, but hydrogels with increased toughness and higher resemblance in their time dependent mechanical properties to natural tissues would be even more beneficial [7, 8]. Thus, as a new approach, in this work our aim was to prepare PVA and muc/PVA hydrogels using different PVAs from the previously used. PVAs with two different degrees of hydrolysis (88% and 98%) and five different molecular weights (61, 125, 130, 195 and 205 kDa) were used.

Firstly, PVA solutions with 15 wt% PVA were prepared and characterised via rotational rheometry. All samples showed shear-thinning, and zero shear viscosity was also calculated by extrapolating viscosity to zero shear. By increasing either the molecular weight or the degree of hydrolysis of the PVA zero shear viscosity increased. From the PVA solutions, hydrogels were synthesized by freezing-thawing method [7, 8, 9]. The hydrogels were characterised via oscillatory rheometry and tensile tests. From PVA which has a lower degree of hydrolysis (88%), hydrogels could not be synthesized. In contrast, from PVA which has a higher degree of hydrolysis (98%), hydrogels were successfully synthesized, and the mechanical properties of the gels could be controlled by changing the molecular weight of the PVA. As the molecular

weight increased, the stiffness, toughness and tensile strength of the hydrogels all increased. Interestingly, while the stiffness continuously increased with the molecular weight, after a certain point, further increasing of the molecular weight did not increase further either the toughness, or the tensile strength. The explanation could be that by increasing the molecular weight the number or size of the crystallites increased, but that did not make any effect on failure under large deformation. The viscoelasticity, and time dependent properties of the hydrogels got more similar to the reference native mucosa (porcine small intestinal mucosa) as the molecular weight of the PVA increased.

After the rheological and mechanical characterisation at large deformation of the PVA hydrogels, PVAs which are the most promising base material for mucosa mimetic materials, were chosen. From these PVAs, PVA and also muc/PVA (5 wt% mucin, 10 wt% PVA) hydrogels were synthesized by freezing-thawing method for the adhesion measurements. The adhesion of commonly used tablet excipients (cross-linked polyacrylic acid (PAA), hydroxypropyl methylcellulose (HPMC) and chitosan) was measured on the hydrogels via tack adhesion test. In case of each molecular weight the strength of the adhesion of PAA was the largest, since it is the stronger adhesive among those were used. The adhesion of HPMC and chitosan were usually not significantly different, but both were much below that of PAA. Also, in most cases, the adhesion of each tablet was stronger on PVA hydrogels, than muc/PVA hydrogels, due to the lubrication effect of mucin. The measured adhesion of the tablets on the hydrogels was comparable to their adhesion on porcine small intestinal mucosa.

To conclude, the PVA hydrogels based on PVA with higher molecular weight were stiffer and tougher than hydrogels, which were synthesized from PVA with lower molecular weight. Moreover, their time-dependent properties were more similar to those of native mucosa and the adhesion of the examined tablets on them was also consistent with the adhesion on native mucosa. Thus, the presented hydrogels are promising mucosa mimetic materials. We plan to vary the muc/PVA ratio of the hydrogels in a wider range to mimic more efficiently the adhesive and viscoelastic properties of the native mucosa.

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Target Agnostic Photoaffinity Labelling by Sulfonylhydrazones

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Photoaffinity labeling is a widely used methodology for interrogating small molecule-protein interactions. However, these applications are limited by the few photo-crosslinkers that typically modify the affinity and the binding mode of the original ligand. In this work, we report the development of new target agnostic photoaffinity warheads, sulfohydrazones that form a reactive carbene upon UV irradiation.[1] Careful optimization of the reaction conditions allowed us to effectively label five different amino acid residues in proteins. Our approach turned biologically relevant hydrazones and sulfohydrazones to intrinsically irreversible covalent binders without structural modifications by photoactivation as demonstrated on monoamine oxidase A (MAO-A) enzyme and STAT5b (Signal transducer and activator of transcription 5b) transcription factor. Sulfohydrazones are readily accessible by transforming the corresponding carbonyl group of a ligand or a suitable tag that extends the application domain of the method for any ligands exemplified by conditional labelling of the acetylcholine esterase enzyme and the oncogenic mutant of GTP-ase $KRas^{G12D}$.

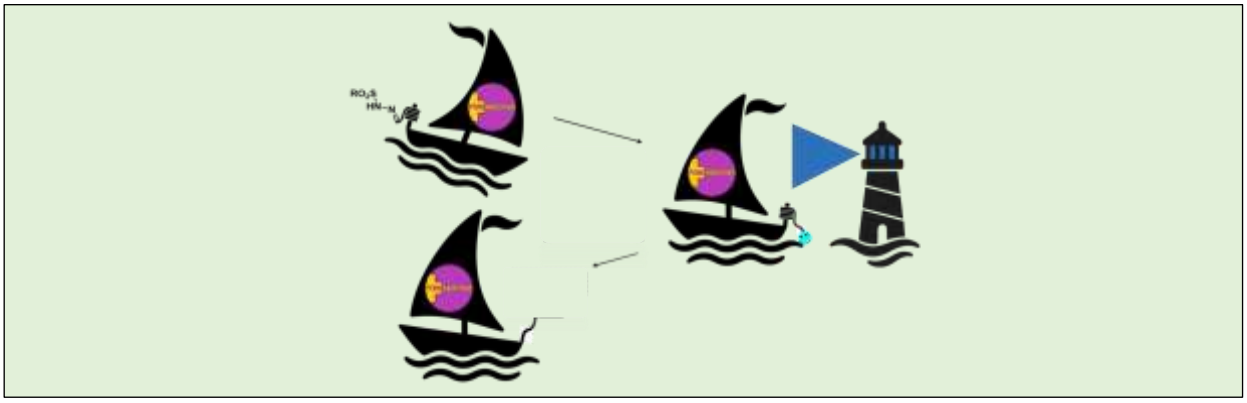

Figure 1. Photoaffinity labeling by sulfonylhydrazones developed by our research group

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ENANTIOCOMPLEMENTARY BIOREDUCTION OF FLEXIBLE RING *N*-(3-OXOBUTYL)-HETEROCYCLES PROVIDING ENANTIOPURE CHIRAL FRAGMENTS FOR DRUG DISCOVERY

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In this study, the bioreduction of prochiral *N*-(3-oxobutyl)-heterocycles comprising various (partially) saturated, flexible rings was explored using whole-cell forms of wild-type yeast strains, commercially available baker's yeast (*Saccharomyces cerevisiae*) and two enantiocomplementary recombinant alcohol dehydrogenases. Initially, four wild-type yeast strains and baker's yeast were screened for ketoreductase activity on a series of nine flexible *N*-heterocycles with prochiral carbonyl group in the *N*-(3-oxobutyl) sidechain. Among the yeast strains tested, *Candida parapsilosis* NCAIM Y.02342 (WY12) proved to be the most effective, resulting in the corresponding (*S*)-alcohols with low to moderate conversions.

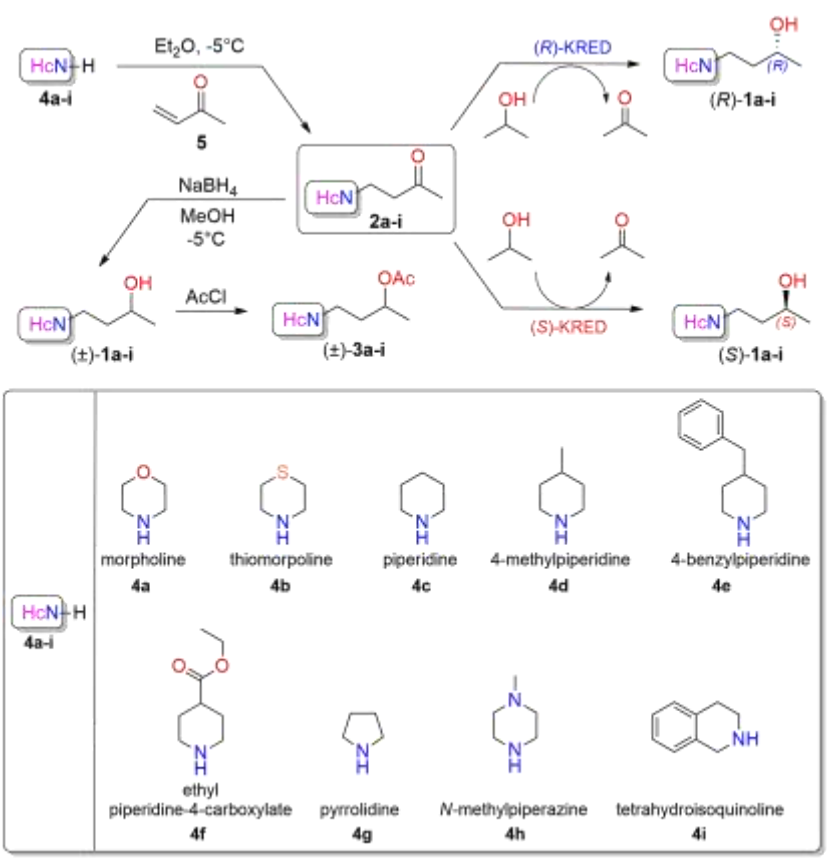

Figure 1. Synthesis of flexible ring *N*-(3-oxobutyl)heterocycles **2a-i** and their chemical and bioreduction to racemic and optically active alcohols (±)-**1a-i**, (*S*)-**1a-i** or (*R*)-**1a-i,** respectively.

Using recombinant alcohol dehydrogenase whole-cell preparations as biocatalysts ((*S*)-selective ADH from *Rhodococcus aetherivorans* (RaADH) and (*R*)-selective ADH from *Lactobacillus kefir* (LkADH)) resulted in higher conversions in most cases, while maintaining the full enantiotopic selectivity. Usually, the preparative scale bioreductions showed comparable or even higher conversions than those observed in the small-scale screening reactions, resulting in virtually enantiopure (*S*)- and (*R*)-alcohols (ee >99%), which are promising chiral fragments with a high degree of drug-likeness. Molecular docking of the *N*-(3-oxobutyl)-substituted heterocycles with flexible rings **2a-i** could be successfully applied to prove the absolute configuration of all the forming alcohols (*S*)-**1a-i** and (*R*)-**1a-i**.

DEVELOPMENT OF AN MNP-BASED SUPPORT REUSABILITY METHOD FOR HIS-TAGGED ENZYME IMMOBILIZATION

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Nowadays, the beneficial catalytic properties of enzymes are used in the food, textile, detergent, paper and fine chemical industries. The immobilization of enzymes can be used to overcome several drawbacks, such as low enzyme stability or limited reusability of the native biocatalyst.[1,2] Several enzyme immobilization methods have been developed in recent decades.[3] Among the several methods developed for enzyme immobilization, the selective enzyme complexation technique based on immobilized metal ion affinity chromatography (IMAC) was used in this study.[4] Theoretically, the metal ion affinity method permits enzyme elution. However, to the best of our knowledge, this has not been documented in the scientific literature regarding the reuse of immobilized enzymes with fresh enzyme solutions.

The reusability of supports subsequent to enzyme inactivation is a subject of considerable interest. The enzyme can be replenished in flow reactors without removing the stationary phase, which enables the use of specialized, expensive supports. In the following study, silica-covered magnetic nanoparticles (MNPs) will be utilized as support, modified with 3-(2-aminoethylamino)propyldimethoxymethylsilane, EDTA and Co^{2+}.[5]

Initially, different eluents were examined using MNP-EDTA-Co^{2+} as support and His_{10}-tagged phenylalanine ammonia-lyase from parsley (*Pc*PAL): 1 M imidazole, 100 mM ethylenediaminetetraacetic acid (EDTA), 100 mM diethylenetriaminepentaacetic acid (DTPA), 5% diethylenetriamine (DETA), and concentrated NaCl solution. Afterward, 3 different acids were tested: acetic acid, oxalic acid, and citric acid. The two most effective eluents, 5% DETA and 1% citric acid, were further investigated. The 5% (pH 11) DETA solution has been shown to gradually inactivate the *Pc*PAL, with residual activity still measurable. The citric acid completely eliminated the enzymatic activity. The 1 M imidazole solution was incapable of removing more, than 71% of the enzyme from the MNP. Nevertheless, enzyme elution has been found to be incomplete in all cases. The reusability experiments were carried out using the MNP support with 5% DETA as the eluent.

Reusability was investigated by subjecting the functionalized MNP (5.0 mg) to five successive cycles of enzyme immobilization and elution. Activity measurements were taken prior to and following each elution cycle. The eluent solutions remove the chelated Co^{2+} ions from the surface. After elution and washing, the MNP-EDTA was coupled with cobalt(II) acetate and the corresponding enzyme. To demonstrate the applicability of the method, two distinct enzymes were tested. In addition to the homotetrameric *Pc*PAL, a homodimeric, (*S*)-selective transaminase from *Vibrio fluvialis* (*Vf*TA) was utilized. The immobilized *Vf*TA was tested in the transamination reaction of racemic 1-phenylethylamine, with sodium pyruvate serving as the amine acceptor. Relative specific biocatalytic activities at 3 min and relative conversions after 1 h were evaluated.

With both biocatalysts, the relative activities and conversions were at or above 80% during the third cycle using 5% DETA as eluent. Not only the reusability was better in the case of the *Vf*TA-MNP, than the *Pc*PAL-MNP, but there were less residual activity, indicating superior elution efficiency. One explanation is the homodimeric structure of the *Vf*TA only contains 2 His-tags compared to the 4 found on the homotetrameric *Pc*PAL, providing less attachment points to the support per molecule. In addition, the His-tag of the transaminase is 6 units long, while that of the PAL is 10 units. This difference in length could offer further insight into the observed discrepancy in elution. Similar results have been observed with 1% citric acid and *Pc*PAL, with superior residual activities during the fifth cycle.

Next, the two catalysts containing immobilized *Pc*PAL and *Vf*TA enzymes were prepared, eluted with 5% DETA solution, and chelated again using the other enzyme. Activity measurements were performed under the same conditions as in the preceding experiment. This method is designed to eliminate residual activity after elution. At one hour, the conversions were 68 ± 2% and 68 ± 4% for *Pc*PAL, 29 ± 1% and 31 ± 2% for *Vf*TA after the first and second immobilization, respectively. Interestingly, immobilization on the support that had already been used resulted in relative conversions of 100% or higher compared to the other catalysts following the initial immobilization. This finding is consistent with the results of the previous experiment, in which no major decrease in conversion occurred over three cycles of transaminase catalysis.

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COMPARISON OF THE STABILIZING EFFECTS OF ELLAGIC ACID AND GALLIC ACID IN POLYETHYLENE

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During the most common plastic processing methods and applications, the oxygen present reacts with the polymer and with the alkyl radicals to create oxygen-centered radicals, which cause further degradation of the polymer chain. One of the largest groups of stabilizers used in plastics is phenolic antioxidants, which donate hydrogen to peroxy radicals, creating hydroperoxide, which hydroperoxide decomposers can decompose. A cause for concern with synthetic phenolic antioxidants is that their reaction products may have an adverse effect on living organisms. In addition, there is a growing demand to replace synthetic materials with natural, renewable raw materials. During our research on natural antioxidants, we found an interesting phenomenon. Pomegranate extract proved to be an excellent processing stabilizer (oxygen-poor environment), but it was not sufficient in oxygen-rich environment (thermooxidative degradation). According to our theory, the presence of the para-position active center has a significant effect on this. In order to prove our theory, we compared the stabilizing efficiency of two natural antioxidants with very different chemical structures. Gallic acid can react with two oxygen-centered radicals; however, because of the lack of a para-H atom, the ellagic acid cannot[1]. We homogenized the stabilizers in polyethylene powder and produced granules from them in six extrusion steps at different concentration levels (0-1000 ppm). The test results show that the number of chain-end vinyl groups and the flow characteristics were very similar for both stabilized materials, indicating that the two additives had a similar effect on the polymer degradation. However, there was a significant difference in the thermooxidative stability of the samples. Based on our results, gallic acid provides greater long-term thermal stability than ellagic acid, which can be explained by the presence of the para-position active center found in gallic acid. Further studies are needed on the mechanism of action of stabilizers. We also examined the effect of the natural antioxidant concentration on the properties of the PE and found the optimal amount of the applied additive.

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TAYLOR DISPERSION ANALYSIS AT HIGH PRESSURE – CHALLENGES AND CORRECTIONS

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High pressure processes are a swiftly developing field of technologies, with processes such as the chemical recycling of polymers, or particle generation technologies for the pharmaceutical industry. The development of such processes is important on the road to sustainability as they contribute to the efforts to create a circular economy and facilitate the substitution of conventional harmful organic solvents. Micro-flow reactors are often utilised in the development of such processes, so their accurate description is often needed for successful development.

In our work, we focus on the unique challenges present in a hydrothermal micro-flow reactor system. In hydrothermal processes, we utilise water at high pressure (4+ MPa) and temperature (200+°C). Under these conditions, water is a versatile and reactive medium with its physico-chemical properties, such as solvent power or reactivity varies greatly with the change of pressure and temperature. While both the typical temperature and pressure values are well within the ordinary range of chemical industry processes, the development and operation of hydrothermal reactors often require special solutions.

One of the most challenging tasks is process analytics with high information density, for which in-line detection of the components is advantageous. For instance, the determination of the residence time distribution (RTD) of a solute in a reactor is crucial, especially in time-sensitive reactions. This measurement requires the highest possible information density, as the distribution in micro-flow reactors is often significantly different than any idealised model. The most viable choice would be in-line detection in the RTD measurements, however, in-line detection in the hydrothermal environment is challenging if not completely unfeasible technically. While in-line detection at ambient conditions is much easier, the result of such monitoring is always affected by downstream unit operations which are responsible for cooling down, depressurizing and such. Therefore, if an accurate and detailed description of the reactor is needed, suitable corrections and calculations are necessary.

In our work, we present a novel RTD measurement concept based on a two-point injection system. The simplified drawing of the hydrothermal reactor system can be seen on Figure. 1.

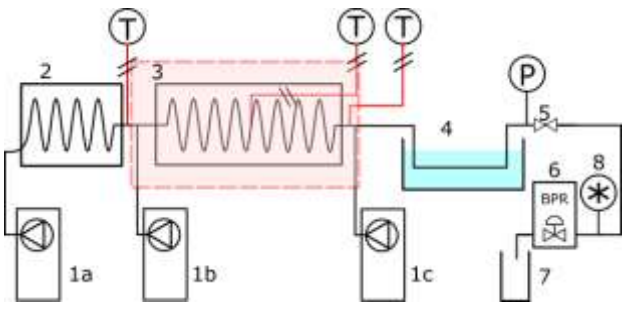

Figure 1. The hydrothermal reactor.

The main goal of the work is the acquisition of the reactor RTD, however, it is impossible to measure it directly. To solve this challenge, two RTDs are measured: the RTD of the whole system (reactor and downstream units), and the RTD of the quench part (downstream units). Since residence time distributions can be interpreted as the transfer function of a unit regarding mass transport, the net residence time distribution of multiple units connected in series can be calculated as the convolution of the individual unit RTDs. Therefore, if the reactor RTD is to be separated from the RTD of the whole system, the mathematical operation of deconvolution is to be calculated.

We developed a novel model-free deconvolution method, which is applicable for this task. We performed RTD measurements at ambient temperature and elevated pressure (5 MPa) with phenol acting as tracer and performed deconvolution on the resulting RTDs to calculate the RTD of the reactor. We performed validation measurements possible at ambient temperature, which showed a good agreement between the calculated and measured reactor RTD. Finally, Taylor-Aris Dispersion as a presumably suitable RTD model was fitted to the measurement results. The fitting showed significantly worse description of the reactor than the result of deconvolution, highlighting the fact that the trade-off of using model-free deconvolution is often a must even at relatively simple systems if an accurate description is needed.

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Quantum Chemical Insight into the Production of Reactive Oxygen Species by Catechol/o-Quinone Redox Cycling: The Case of 4-Hydroxyestrogens

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Hormone replacement therapy (HRT) has been employed for nearly a century to alleviate menopausal symptoms in women; however, long-term studies have revealed that it also represents a significant risk factor for hormone-dependent cancers.[1] Evidence suggests that estrogens in HRT may exert their harmful effects through their catechol metabolites. When estrogens are metabolized, one of the possible pathways yields catechol estrogens. Catechols (QH_2) primarily exhibit toxicity through oxidation to quinones (Q), a process in which molecular oxygen serves as the oxidant, generating superoxide radicals ($O_2^{\bullet -}$).[2] These reactive species inflict damage on DNA and proteins, and their production is amplified by the reduction of quinones back to catechols, thereby sustaining the cycle.

The rate of superoxide generation varies among different catechols. To better understand and predict this toxicity, it is essential to establish structure–reactivity relationships. In this work, we propose a quantum chemical approach to evaluate catechol toxicity through redox cycling. We calculated the barriers of the elementary steps (proton-, electron-, and hydride transfer steps) involved in redox cycling and propose a model to take cellular concentrations into account to predict toxicity. The method is applied to three catechol estrogen metabolites: 4-hydroxyestrone (E), 4-hydroxyequilin (Eq), and 4-hydroxyequilenin (Eqn), as illustrated in Figure 1.

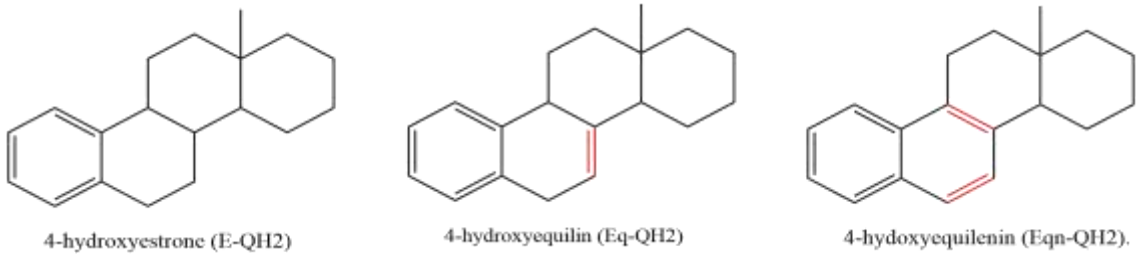

Figure 1. Structure of 4-hydroxyestrone (E-QH2), 4-hydroxyequilin (Eq-QH2), and 4-hydroxyequilenin (Eqn-QH2). Unsaturated bonds of ring B are shown in red.

After identifying the elementary steps of O_2 reduction (Figure 2), we analyzed the thermodynamics of the cycle using key parameters: acidity (pKa), standard reduction potential (ε^0), and hydricity (H^-) of the catechol derivatives.

The results indicate that the rate of redox cycling between Eqn-QH_2 and Eqn-Q is superior to that of E and Eq. Nevertheless, thermodynamic data alone offer only qualitative insights.

To achieve quantitative assessment, we further investigated the kinetics of catechol/quinone cycling by calculating standard activation Gibbs free energies ($\Delta G^{\ddagger 0}$) using DFT. The results show that Eqn-QH_2 undergoes autoxidation more readily than E-QH_2 and Eq-QH_2. Since $\Delta G^{\ddagger 0}$

neglects protonation effects and reaction rates are strongly dependent on protonation state, we also calculated effective activation Gibbs free energies (ΔG‡°_eff), incorporating both pKa values and reactant concentrations. These results establish the toxicity ranking among estrogen catechols as: E-QH_2 < Eq-QH_2 <<< Eqn-QH_2.

We further examined catechol/quinone redox cycling in the presence of Cu^{2+} ions. Copper(II), a stronger oxidant than O_2, reduces the barriers for electron transfer and thus accelerates reaction rates. Specifically, ΔG‡° and ΔG‡°_eff of ET-1a decrease by approximately 5–6 kcal/mol when Ex-C reacts with Cu^{2+} instead of O_2. Despite this, effective barriers remain relatively high for E and Eq but low for Eqn. Collectively, our findings show that redox cycling and reactive oxygen species (ROS) formation—and consequently toxicity—follow the order: Eqn >> Eq > E. Integrating computational thermodynamic and kinetic data with effective barrier analysis offers a powerful framework for assessing the cytotoxic potential of catechol/quinone redox systems.

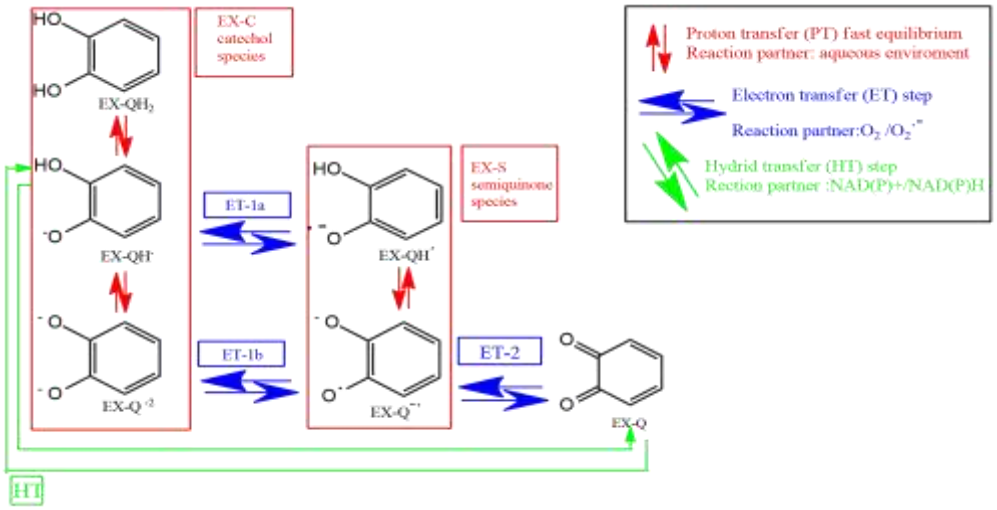

Figure 2. Elementary steps of redox cycling (only the aromatic ring "A" is depicted for clarity; the rest of the compounds are omitted). Proton transfer steps are assumed to be in rapid equilibrium under aqueous conditions. ET-1a and ET-1b denote the two possible one-electron oxidation reactions of the catechol species, while ET-2 corresponds to semiquinone oxidation to quinone.

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CONTINUOUS-FLOW SYNTHESIS OF ARIPIPRAZOLE THROUGH THE SAFE UTILIZATION OF TETRAHYDROFURAN HYDROPEROXIDE

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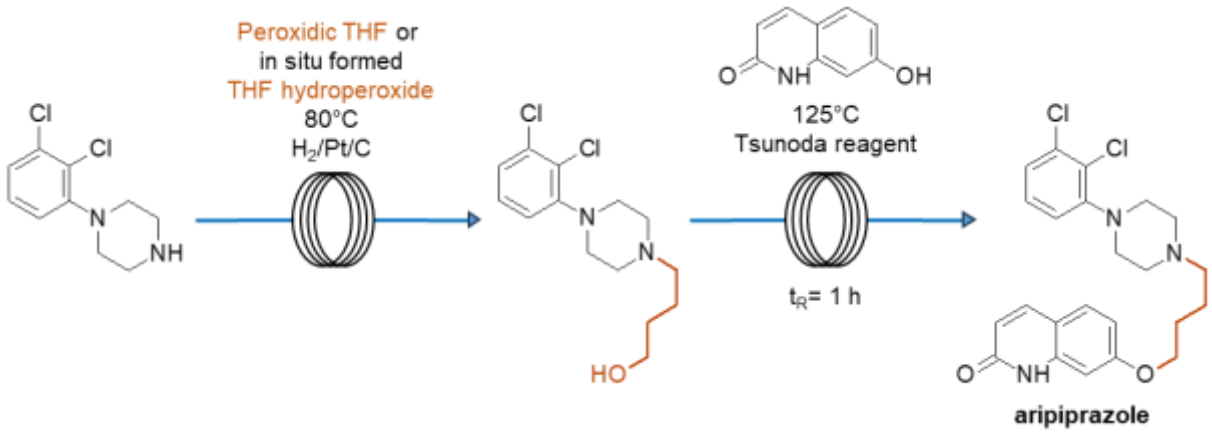
Aripiprazole is a globally prescribed atypical antipsychotic, indicated for schizophrenia, bipolar disorder, and major depressive disorder. Given its widespread use and generic availability, the development of sustainable and efficient synthetic methods have high relevance.

We have designed a novel, continuous-flow synthesis of aripiprazole, featuring a rarely utilized *N*-hydroxybutylation step with tetrahydrofuran (THF) hydroperoxide. This transformation was successfully adapted to flow conditions, enabling rapid and safe conversion through controlled thermal activation of the peroxidic mixture. High productivity was achieved using in situ generated THF hydroperoxide. Following an off-line work-up, the *N*-hydroxybutylation step was semi-continuously integrated with a continuous Mitsunobu reaction towards aripiprazole employing the Tsunoda reagent. The resulting process offers a more environmentally benign alternative to the conventional batch synthesis,[1] highlighting the potential of flow chemistry in green pharmaceutical manufacturing.



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STATISTICAL ASSESSMENT OF CONTENT UNIFORMITY TESTING USING CONVENTIONAL AND PROCESS ANALYTICAL TECHNOLOGY -BASED ANALYTICAL METHODS

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The manufacture and marketing of pharmaceutical products – overall, their quality assurance – are strictly regulated by the authorities. One of the most critical aspects of this is the testing of content uniformity (CU) of the active substance. Recently, a new approach has emerged in the field of quality assurance for process testing, based on the application of Process Analytical Technology (PAT) and Quality-by-Design (QbD) principles. While following these principles offers numerous opportunities for more efficient and faster production cycles, their application in current regulatory systems also poses a number of challenges.

One of the objectives of this research is to present the statistical qualification procedure used in the current regulatory system. In addition, we examine the questions raised in this area by the use of newer analytical methods that enable continuous monitoring, such as near-infrared spectroscopy (NIR). In our computer simulations, large production batches containing 10^7 tablets were modeled, with varying expected values and variances for active pharmaceutical ingredient (API) contents. Samples were taken ranging from 30 to 10^7 units with 10,000 repetitions from these. Based on these simulations, the probability that an entire batch could be considered acceptable, i.e., suitable for release, was determined.

Our investigation covered the presence of a given degree of error resulting from analytical measurement, as well as its combined effect with the sample size on the probability of acceptance of the entire batch. Our aim was also to answer the question of what sample size is required for analytical methods supporting continuous monitoring in order to achieve at least the same level of performance during assessment as with traditional HPLC-based methods.