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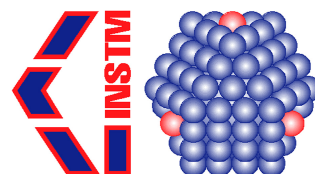
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SCIENTIFIC PROGRAM

The conference presentations consist of keynote lectures (KN), invited lectures (IL) and oral communications (OC).

Monday, March 11th, 2019

11:00 REGISTRATION

13:00 OPENING CEREMONY

Elisabetta Ranucci, Università di Milano (I), Congress Chair

Laura Prati, Università di Milano (I), Head of the Chemistry Department

Chairperson: Paolo Ferruti, Università di Milano (I)

13:20 KN **Gaetano Guerra**, University of Naples Federico II (I).

Nanoporous crystalline polymers and industrial innovations

14:00 IL **Simon C.W. Richardson**, University of Greenwich (UK)

The use of biopolymers for siRNA and antisense intracellular delivery

14:20 IL **Nicola Tirelli**, Istituto Italiano di Tecnologia, Genoa (I)

Polysulfides as oxidation-sensitive macromolecules – Mechanisms and applications

15:00 IL **Paweł Chmielarz**, Rzeszów University of Technology (PL)

Electrochemically mediated atom transfer radical polymerization (eATRP)

15:20 IL **Mario Malinconico**, Institute for Polymers, Composites and Biomaterials IPCB-CNR, Napoli-Portici (I)

IUPAC 100 years serving chemistry

15:35 COFFEE BREAK

Chairperson: G. Guerra, University of Naples Federico II (I)

15:55 KN **Francesco Cellesi**, Polytechnic University of Milan (I)

Macromolecular design in nanomedicine. The role of polymer architecture and functionality in overcoming biological barriers

16:35 OC **Daniela Maggioni**, Università di Milano (I)

Unique trafficking to the cell cytosol and to the nucleus of a luminescent linear polyamidoamine-ruthenium complex

16:50 IL **Filippo Rossi**, Polytechnic University of Milan (I)

Three dimensional biomimetic hydrogel to deliver factors secreted by human mesenchymal stem cells in spinal cord injury

17:10 IL **Tina Vermonden**, Utrecht University (NL)

Balancing hydrophobic and electrostatic interactions in thermosensitive polyplexes for

nucleic acid delivery

- 17:30 OC **Roberta Cavalli**, Università di Torino (I)
Advanced drug nanodelivery systems based on synthetic copolymers for treatment of infectious diseases
- 17:45 OC **Emanuele Mauri**, Campus Bio-Medico di Roma (I)
Chemical and physical functionalization of nanogels for controlled intracellular drug release
- 18:00 OC **Roberto Santoliquido**, Alfatest (I)
Detection of single block impurities in AB block-copolymers by gel permeation chromatography and ultra high performance liquid chromatography
- 18:15 OC **Giulia Risi**, Università di Pavia (I)
Bioprintable hyaluronic acid-based hydrogels for 3D in vitro studies
- 18:30 **END OF SESSION**

Tuesday, March 12th, 2019

08:30 REGISTRATION

Chairperson: Nicola Tirelli, Istituto Italiano di Tecnologia, Genoa (I)

- 09:30 KN **Minna Hakkarainen**, Royal Institute of Technology (SE)
Carbon dot modified nanocomposites and hydrogels
- 10:10 IL **Debora Berti**, University of Florence (I)
Self-assembly of lipids and block copolymers as a new route towards functional nanomaterials
- 10:30 OC **Dagmar R. D'hooge**, Ghent University (BE)
How side reactions can influence poly(2-oxazoline) synthesis for polymer therapeutics and hydrogels
- 10:45 OC **Camilla Parmeggiani**, University of Florence (I)
Liquid crystalline polymers for regenerative medicine and tissue repair

11:00 COFFEE BREAK

Chairperson: F. Cellesi, Polytechnic University of Milan (I)

- 11:20 KN **Vitaliy Khutoryanskiy**, University of Reading (UK)
Designing novel polymeric materials for transmucosal drug delivery
- 12:00 IL **Gianluca Ciardelli**, Politecnico di Torino (I)

Biomedical polyurethanes design, synthesis and processing: a (possible) success story of polymer chemistry towards the bedside

12:20 KN **Dieter A. Schlüter**, ETH Zürich (CH)

2D Polymers: synthesis in single crystals and on water

13:00 LUNCH AND POSTER SESSION

Chairperson: M. Hakkarainen, Royal Institute of Technology (SE)

14:10 IL **Orietta Monticelli**, University of Genoa (I)

Novel formulations based on polylactic acid for biomedical applications

14:30 OC **Federica Lazzari**, Università di Milano (I)

D-, L-arginine derived polyamidoamino acids and sodium deoxycholate: the importance of self-assembly in chiral recognition

14:45 IL **Elisa Passaglia**, Institute for Chemistry of Organometallic Compounds ICCOM-CNR, Pisa (I)

2D hybrid substrates for functional polymer-based materials

15:05 IL **Andrea Dorigato**, University of Trento (I)

Investigation of the physical behaviour of multifunctional polymer composites with thermal energy storage/release capability

15:25 OC **Martin Wortmann**, Bielefeld University of Applied Sciences (DE)

Formation of an interpenetrating polymer network of polyurea and silicone rubber in the vacuum casting process

15:40 OC **Marco Coletti**, TA Instruments-Waters (I)

Dynamic rheological characterisation of silicones for podiatry applications

15:55 COFFEE BREAK

Chairperson: V. Khutoryanskiy, University of Reading (UK)

16:15 KN **Monika Österberg**, Aalto University (FI)

Novel functional materials from lignocellulosic polymers: surface engineering of nanoparticles and applications

16:55 IL **Giovanna Buonocore**, Institute for Polymers, Composites and Biomaterials IPCB-CNR, Napoli-Portici (I)

Innovative materials for active packaging: Antimicrobial release from inorganic carrier embedded into polymer films

17:15 IL **Antonella C. Boccia**, Institute for macromolecular studies ISMAC-CNR, Milan (I)

Structural characterization of renewable natural and synthetic polymers for active applications

17:35 OC **Richard d'Arcy**, Istituto Italiano di Tecnologia, Genoa (I)

Super strong enzymes. Polysulfides as sacrificial stealth components of protein conjugates

17:50 OC **Mohamed Yassin**, National Research Center (EG)

Smart polymeric carriers tailored towards biotechnological applications

18:05 **END OF SESSION**

19:30 **SOCIAL DINNER**

Wednesday, Marh 13th, 2019

Chairperson: D. N. Bikiaris, Aristotle University of Thessaloniki (GR)

09:30 OC **Tao Zou**, Aalto University (FI)

Chitosan-coated colloidal lignin particles as novel stabilizers for Pickering emulsion

09:45 OC **Giuseppe Cappelletti**, Università di Milano (I)

Fluorine-modified polyacrylic coatings for cultural heritage protection

10:00 OC **Lorenzo Migliorini**, Università di Milano (I)

From artificial to natural-derived electroactive hydrogels: materials for soft actuation, microfluidics, biotechnology

10:15 OC **Jurgen E. K. Schawe**, Mettler-Toledo AG (CH)

The influence of fillers and nucleating agents on polypropylene crystallization at high supercooling measured by Fast DSC

10:30 **COFFEE BREAK**

Chairperson: M. Österberg, Aalto University (FI)

10:50 KN **Dimitrios N. Bikiaris**, Aristotle University of Thessaloniki (GR)

Phosphorus containing polymers as flame retardants

11:30 IL **Michelina Soccio**, Università di Bologna (I)

Structure, dynamics and barrier performance relationship in furan-based polyesters

11:50 IL **Sophie Guillaume**, Institut des Sciences Chimiques de Rennes CNRS - Université de Rennes 1 (F)

Poly(hydroxyalkanoate)s (PHAs) architectures by ring-opening polymerization of functional β -lactones

12:10 IL **Andrea Pucci**, University of Pisa (I)

Polymers with aggregation-induced emission: a land of opportunities

12:30 **END OF CONGRESS, BEST POSTER AWARDS and CLOSING REMARKS**

KEYNOTES

Synthesis and properties of novel polyesters prepared from furan dicarboxylic acid and vanillic acid biobased monomers

Dimitrios N. Bikiaris

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Bio-based polymers have gained high interest the last decades due to the increased concern about diminishing fossil resources and their impact to global warming. According to IUPAC, a biobased polymer is a polymer derived from biomass or issued from monomers derived from biomass and at some stage of its processing into finished products, can be shaped by flow. All these led to the development and growth of a new economy known as bioeconomy, and the first bio-based polymers introduced in the market were poly(hydroxy alkanoate)s produced by ICI (GB) in the 1980s. Historically, the raw materials basis was substantially renewable, with the utilization of biomass and coal being equal about 100 years ago. In the 1920s, coal tar-based materials had taken the lead, reaching a maximum around 1930. Thereafter, fossil gas and oil irresistibly took over, eliminating coal nearly completely and reducing renewable feedstocks to very modest levels. After 2000 there is a great interest for materials derived from renewable resources and these demands will increase in the next years. The production and commercialization of renewable bio-based polymers is expected to continuously grow.

Biobased materials offer interesting solutions due to their useful functional properties and provide positive impacts on society: low carbon footprint, wider supply base than oil based chemicals, less influenced by fluctuations in oil price, reduction in waste production and landfill use, job positions in rural areas, promoting of the balance between agricultural areas and forests. There are different strategies to produce bioplastics from biomass. The chemical modification of natural existing polymers is first employed with the intent of improving or tuning their pristine properties. Biorefining of biomass also takes place to produce synthetic crude oil ("renewable oil") and green monomers. These monomers can be used for the synthesis of already known polymers, or the for synthesis of new polymers with novel properties in order to replace already existing ones. Today, there are plenty such monomers available, most of them being diols and diacids.

2,5-Furandicarboxylic acid (2,5-FDCA) and vanillic acid (VA) are two of the most important diacids for the production of biobased polyesters. During the last decade significant progress has been made towards the synthesis of 2,5-FDCA polyesters with different biobased diols and several problems on the aspects of synthesis and properties have been successfully overcome. However, some important problems associated with synthesis of polyesters with high molecular weight have to be solved first in order to make them appropriate for industrial applications, specifically their weak mechanical properties and coloration. To this direction, high purity monomers, stabilizers and new catalysts are under investigation by the research community and industries with promising results. VA, compared with 2,5-FDCA, is an asymmetric molecule and thus its polyesters are prepared in a lower extent. Also, lower reactivity of the secondary hydroxyl group imparts an additional difficulty for the production of such polyesters. However, VA can be polymerized with several diols and aliphatic polyesters as comonomers via solution or melt polycondensation techniques producing completely different polyesters. These are amorphous or crystalline materials and their structural, chemical and physical properties are under investigation.

Macromolecular design in nanomedicine. The role of polymer architecture and functionality in overcoming biological barriers

Francesco Cellesi

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A major challenge in nanomedicine is to enhance drug transport across biological barriers, which are designed by nature to prevent undesired access of molecules to sensitive organs, tissues, cells. Recent advances in polymer chemistry has led to a fine control of key physicochemical properties of polymer nanocarriers, such as size, drug loading and functionality, with the purpose of successfully overcoming these barriers, for an efficient site-specific delivery.

This talk will cover our recent work on the design of biocompatible polymers with complex, well-defined architectures and functionality, which were used to obtain size-tuneable, amphiphilic and multifunctional drug-loaded nanocarriers. A combination of controlled living polymerisations (ROP^{1, 2} and ATRP^{1, 2}) and further derivatization by click-chemistry³ allowed the development of bioactive and traceable nanomaterials which selectively cross specific barriers, including the glomerular filtration barrier to treat chronic kidney diseases, the blood brain barrier to target brain tumors, and specific cell membranes to obtain intracellular drug delivery and/or controlled immunostimulation.

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Acknowledgments

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Nanoporous crystalline polymers and industrial innovations

Gaetano Guerra, Christophe Daniel, Paola Rizzo, Vincenzo Venditto

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For two commercial thermoplastic polymers, syndiotactic polystyrene (s-PS) [1-3] and poly(2,6-dimethyl-1,4-phenylene)oxide (PPO) [4,5], crystalline phases including empty cavities of molecular size in their unit cell have been obtained and named *nanoporous-crystalline* phases. These nanoporous-crystalline phases exhibit density lower than the corresponding amorphous phases and are obtained by guest removal from co-crystalline host-guest phases, between a polymer host and low-molecular-mass guest. Nanoporous-crystalline phases are able to absorb guest molecules also from very dilute solutions. Most studies have been devoted to s-PS, which exhibits two different nanoporous-crystalline phases, δ^1 and ϵ ,² whose nanoporosity is organized as isolated cavities and channels, respectively. Physically crosslinked monolithic aerogels, whose physical knots are crystallites exhibiting a nanoporous crystalline form, will be also discussed [6,7]. These *aerogels* present beside disordered amorphous micropores (typical of all aerogels) also all identical nanopores of the crystalline phases. Their outstanding guest transport properties combined with low material cost, robustness, durability and easy of handling and recycle make these aerogels suitable for applications in chemical separations, purification and storage [6,7]. Most of the presentation will be devoted to possible industrial innovations based on materials with co-crystalline and nanoporous crystalline s-PS phases. In particular, applications of nanoporous films for active packaging of fruit and vegetable (by removal of ethylene and carbon dioxide) [8], of nanoporous staple for removal of pollutants from water and air [9] and of nanoporous aerogels as support for nanostructured catalysts [10], will be presented.

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Carbon dot modified nanocomposites and hydrogels

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Biobased carbon dots (C-dots) have captivated tremendous interest due to a palette of attractive properties from favorable biocompatibility to intriguing optical properties. The potential of C-dots as multifunctional polymer additives is also extremely promising. We have demonstrated a facile microwave-assisted route for preparation of carbon spheres (C-spheres) from various biopolymers [1] and waste products [2,3]. Multifunctional zero-dimensional nano-graphene oxide (nGO) and reduced-nGO (r-nGO) type C-dots were further derived from the C-sphere intermediates [4]. These C-dots were shown to be valuable property enhancers and bioactivity inducers in starch, polylactide (PLA) and polycaprolactone (PCL) based packaging films [3,5] and biomedical scaffolds [6,7]. nGO and r-nGO both demonstrated good biocompatibility and attractive bioactivity inducing hydroxyapatite mineralization on the surface of otherwise bio-inert materials. C-dots could also improve the processability and stabilize and reinforce the prepared nanocomposite films [8] and 3D scaffolds [6,7]. nGO surface functionalized 3D scaffolds were further shown to possess drug loading and delivery capacity as well as ability to induce mineralization [9]. We also demonstrated the value of nGO during fabrication of fully biobased chitosan hydrogels for wastewater purification [10,11]. Macroporous chitosan hydrogels were synthesized by crosslinking chitosan with genipin. The inclusion of nGO catalyzed the crosslinking reaction, improved the mechanical properties and increased the adsorption capacity of the formed hydrogels towards trace pharmaceuticals. C-dots are promising additives for wide range of polymer applications improving multiple properties and inducing new ones.

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Designing novel polymeric materials for transmucosal drug delivery

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Mucosal membranes are wet surfaces lining human eye, airways, gastrointestinal and urogenital tracts. Drug delivery via mucosal surfaces offers a number of advantages including ease of therapy administration and termination, improved drug bioavailability, and possibility of targeting particular organs [1]. Dosage forms for transmucosal drug delivery should either be able to stick to mucosal surfaces and retain on them (mucoadhesion) or be able to penetrate through mucus layer to reach epithelial cells (mucopenetration). This lecture will describe the design and characterisation of polymeric materials with enhanced ability to adhere to mucosal surfaces or enhanced ability to penetrate through mucosal barriers. A range of novel mucoadhesive polymeric materials were synthesised to have special functional groups such as thiol- [2], acrylate- [3], methacrylate- [4] and maleimide- [5,6] capable of forming covalent linkages with thiol groups present in mucins on mucosal surfaces. Mucopenetrating materials should have inert and stealthy surface chemistry [7]. We have developed mucopenetrating nanoparticles using thiolated silica decorated with poly(2-oxazoline) short chains [8,9] and demonstrated that the nature of pendant groups strongly affects the ability of nanomaterials to penetrate. The application of these mucoadhesive and mucopenetrating polymeric systems for ocular, gastrointestinal and intravesical drug delivery will be discussed.

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Novel functional materials from lignocellulosic polymers: surface engineering of nanoparticles and applications

Monika Österberg

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There is extensive ongoing research on functional materials based on cellulose nanofibrils (CNF). These include e.g. barrier materials, printed electronics, sensor materials and hydrogels for tissue engineering, to name a few. In contrast, the second most abundant renewable plant polymer, lignin, is still underutilized in material applications. However, recent advances in understanding fundamental properties of lignin have paved the way for the fabrication of colloidal lignin particles (CLPs) with controlled morphologies. Breakthroughs in particle preparation processes allow for preparing CLPs in a scalable manner directly from unmodified lignin [1,2]. In this presentation we will give some examples of surface modification and applications of CNF, CLPs and their combinations. Common for all the examples are that, controlling the surface interactions have been essential to achieve the optimal performance. The modifications have also all followed principles of green chemistry and striving for simple and scalable approaches. Simple mixing with sodium bicarbonate enables production of eco-friendly fire-retardant CNF aerogels suitable for insulation [3]. Very stable Pickering emulsions were prepared by adsorbing soluble cationic lignin onto anionic CLPs [4]. These cationic CLPs could also be used for immobilization of enzymes and enabling efficient esterification in aqueous media [5]. Lastly, we demonstrate how these natural nanoparticles can be combined to prepare ductile composites resistant to oxidation and with UV-shielding properties while still semitransparent [6]. Lignin is usually combined with brittleness, but here the spherical lignin particles acted as ball bearing lubricants and stress transferring agents in the CNF matrix. We envision that by combining these two renewable nanoparticles, novel sustainable materials with application possibilities in food packaging, water purification and biomedicine will be developed (Fig 1).

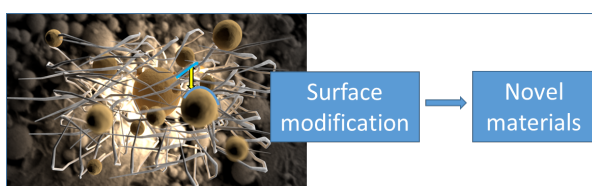


Figure 1. By tuning the interfacial interactions between lignocellulosic nanoparticles novel high performance materials can be developed.

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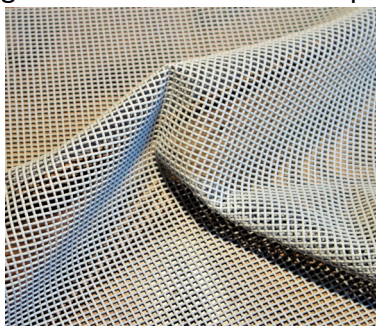
2D polymers: Synthesis in single crystals and on water

Dieter Schlüter

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Two-dimensional materials (2DM) are sheet-like entities and of great interest for their manifold properties. Famous representatives are graphene, boronitride or molybdenum disulfide. 2DMs are often provided by nature or are obtained under harsh conditions. Such conditions exclude the synthetic arsenal of organic chemistry to be used for rational sheet creation, sheet structure variation and sheet engineering on a molecular level.

Recently it was shown that covalent monolayer sheets can be accessed at room temperature by genuine two-dimensional polymerization of organic monomers applying simple protocols. They include spreading of monomers at an air/water interface into long-range ordered reactive monolayer packings or crystallizing them into layered single crystals, followed by light-induced growth reactions. These growth reactions result in macroscopic sheets of considerable mechanical strength, whose structures resemble molecular fishing nets (2D polymers). The photograph shows a conventional laboratory mat, which, on a macroscopic scale, has the necessary features of a 2D polymer.



The contribution addresses strategic, synthetic and analytical issues and provides a view into the future.

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***INVITED LECTURES
&
ORAL COMMUNICATIONS***

Structural characterization of renewable natural and synthetic polymers for active applications

Antonella C. Boccia

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Worldwide 335 million tons of plastic materials are produced annually and nowadays, a world without synthetic polymers seems unimaginable [1]. But plastics are “almost” forever thus resulting in a negative impact on the environment through water and land pollution. Stringent environmental regulation has led to a growing interest in natural based polymers representing an alternative to the conventional materials. In this context starch deriving from biomass is an excellent candidate for the production of natural based polymers being one of the most abundant biopolymer on earth nevertheless the material suffers of some disadvantages deriving from an excessive rigidity and affinity for water [2]. In this study starch deriving from the pea pods, (*Pisum sativum*) was used as starting material for the preparation of polysaccharide-based material and, to overcome the above reported limitations, an enzymatic modification with the laccase/TEMPO system was performed [3]. The structure of the modified starch was extensively characterized by means of mono- and two-dimensional NMR spectroscopic experiments. Successively, the modified polysaccharide was lyophilized leading to a compact aerogel characterized by a morphology with irregular pores of dimensions ranging from 200 nm to few microns. The synthesized aerogel was successfully used as carrier of active molecules and the profile of release determined by proton NMR studies.

Innovative materials for active packaging: antimicrobial release from inorganic carriers embedded into polymer films

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One of the possible approaches to delay or inhibit the mechanisms responsible for the degradation of the packed foodstuff is the development of active packaging materials exhibiting a slow and controlled release of active compounds from the film/container to the food. This strategy presents the advantage to overcome the drawbacks related to direct addition of antimicrobial or antioxidant compounds into the food.

Due to recent progresses in material chemistry and material science, advanced nanoscale systems used to control the release of active compounds have recently received tremendous attention. In recent years, many inorganic nanomaterials used as nanocarriers have been intensively studied. Among these, many investigation efforts focused on the exploitation of the porous network provided by such materials as a reservoir for the accommodation of drug molecules. In fact, the well-known opportunity to chemically functionalize the surface of siliceous mesostructures with different organic moieties constitutes a route for controlling the drug release by diffusion under specific conditions. Drug release from mesoporous materials is generally controlled by diffusion. Nevertheless, when the interactions between desorbing molecules and silica pore walls are significantly strong and/or show some kind of specificity, the release also depends on the stability of the complex between the functional groups of the drug and those of the substrate. This phenomenon allows then to fine tune the release of specific molecules from a given mesostructure by simply changing the functional groups attached to its pore walls during the synthesis process. In addition to the production of smart drug delivery systems, such approach can be also used in the field of food packaging due to the increasing interest in the concept of “active packaging” materials as compounds which, interacting with the packaged foodstuff, are able to control its quality as well as to increase its shelf-life.

In this work we present an overview and a comparison of the release kinetics from active polymer films of various active compounds embedded or supported into/onto three inorganic carriers: SBA (Santa Barbara Amorphous), Montmorillonite and Halloysite. Migration tests were performed at 25 °C, using 96% v/v ethanol and water as food simulant, using polymer films obtained by embedding active inorganic carriers into LDPE, chitosan and PCL matrices. Obtained results show the influence of functionalization of the inorganic carriers on the diffusion of active compounds and thus on their release kinetics into the liquid media.

Fluorine-modified polyacrylic coatings for cultural heritage protection

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Deterioration phenomena of ancient and modern stone cultural heritage are natural and unrestrainable decay processes mainly arising from water percolation into stone building materials [1]. Thus, the application of hydrophobic coatings to stone surfaces is mandatory to protect them from the deleterious effects of water exposition. Hence, the aim of the present work was to synthesize new polymeric coatings as stone protective with satisfactory water repellency and improved durability, thanks to the combined use of fluorinated and long alkyl chain monomers and without the use of any photo-stabilizers agents.

Herein, new types of polymer protectives were prepared via free radical polymerization between either 1H,1H,2H,2H-Perfluoro-octyl-methacrylate (POMA) and methacrylic monomers (methyl, MMA, and n-butyl, nBuMA, methacrylates) [2,3]. Specifically, POMA was synthesized via esterification reaction using methacryloyl chloride and 1H,1H,2H,2H-perfluoro-1-octanol. The properties of the home-made hydrophobizing polymers in terms of macromolecular structure, molecular weights, thermal features and water repellency were determined. Furthermore, the long-term behavior of these polymers was estimated by means of accelerated aging tests exploiting UV radiations. Their behavior over time was checked via Size Exclusion Chromatography (SEC) by evaluating M_n and D data of aged polymeric samples and by Fourier Transform Infrared (FT-IR) spectroscopy. By evaluating M_n and D data, all the synthesized polymers seem to be unaffected by UV aging. Thus, the present stable resins were applied on both natural (Botticino marble) and artificial (mortar) stone substrates and their wetting properties together with their absorption by capillarity and water vapour permeability were successfully assessed and compared (Figure 1). All the covered substrates show an increase of water contact angle of around 50° and a decrease in water absorption and permeation of about 50% and 20%, respectively. Hence, the use of these polymer resins can be a way to create tailor-made water repellent materials.

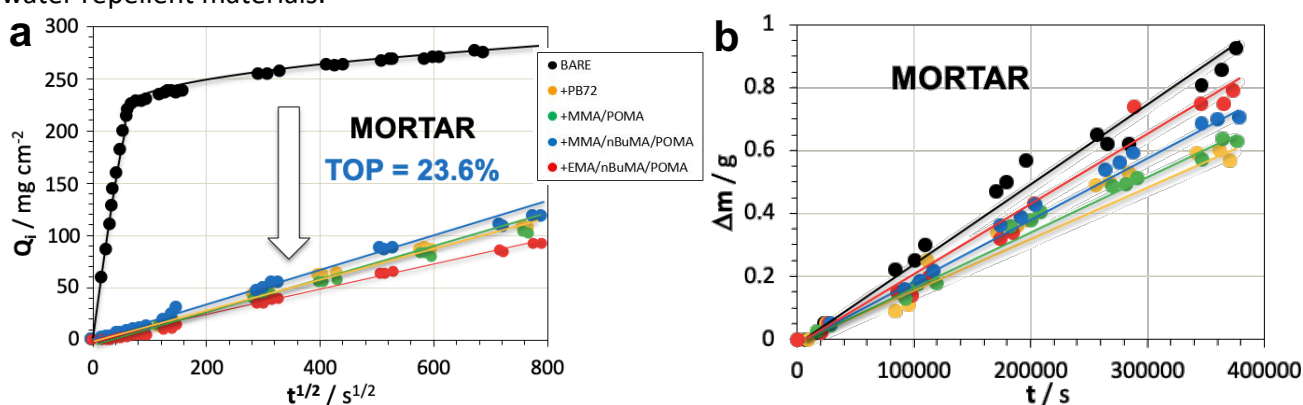


Figure 1. a) Water absorption by capillarity; b) water vapor permeability tests.

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Advanced drug nanodelivery systems based on synthetic copolymers for treatment of infectious diseases

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A number of nano-sized drug delivery systems have been developed with synthetic copolymers for the treatment of infectious diseases, including nanoparticles, micelles, nanovesicles.

The therapy of infections could be improved with nanocarrier formulations. Indeed, the nanomedicine rationale can be exploited to overcome the limitations associated with antibacterial antifungal and antiviral drugs taking into consideration the narrow therapeutic indices, high doses, and frequent administration needed for a number of drugs due to their limited aqueous solubility, short half-life, and/or slow uptake by the body tissues.

In particular polymeric nanoparticles can be loaded with both lipophilic and hydrophilic drugs tuning the molecular architecture, and different loading approaches have been proposed, including covalent chemistry, hydrophobic/electrostatic interactions and entrapment.

Polymer structure plays a key role for the release mechanism of drugs.

Various amphiphilic copolymers with strong hydrophobic chains (i.e. polylactic acid, PLA, polyamino acids, polycaprolactone, PCC, polylactic-co-glycolic acid, PLGA) and hydrophilic portions (i.e. PEG) have been studied for the delivery of drugs for the treatment of infectious diseases.

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Electrochemically mediated atom transfer radical polymerization (eATRP)

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In the last decade, there have been increasing research activities in the use of atom transfer radical polymerization (ATRP) to prepare well-defined polymers [1,2]. ATRP is one of the most rapidly developing areas of polymer science that allows control over molecular weight (MW), preparation of polymers with narrow molecular weight distributions (MWDs), incorporation of precisely placed functionalities, and fabrication of various architectures [3].

Significant efforts have been dedicated to the green chemistry class of this approach. With the advent of methodologies to (re)generate active polymerization catalysts by reduction of deactive catalyst form, ATRP can be conducted at parts per million (ppm) levels of transition metal using a different reducing agents (organic as glucose [4], phenols [5], ascorbic acid [6], hydrazine [5], but also inorganic such as tin(II) 2-ethylhexanoate [4] or zerovalent metal as Ag^0 [7]) in activators regenerated by electron transfer (ARGET) approach, adding zerovalent metals (Cu^0 , Zn^0 , Mg^0 or Fe^0) as supplemental activators and mild reducing agents (SARA) [8] and applying a reducing current as in electrochemically mediated ATRP (eATRP) [9]. Each of these ATRP methods offers a more environmentally benign and industrially relevant alternative for synthesizing polymers compared to normal ATRP [10]. The newest low ppm ATRP method, eATRP [11-13], offer possibility of elimination of chemical reducing agents, and creation catalyst recycle opportunity, and provides an option to receive polymers with well-controlled MWDs [10]. The idea of eATRP technique is that the activator/deactivator concentration ratio is well-controlled by electrochemistry, what is an explanation of the fast development of this method [11].

The main objective of this study is to present recent advances in eATRP in relation to the synthesis of well-defined materials with different architecture and composition, such as consisting of the hydrophilic core and the amphiphilic arms. The general concept of this method will be overviewed, followed by discussion of mechanism, apparatus, advantages and limitations.

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Biomedical polyurethanes design, synthesis and processing: a (possible) success story of polymer chemistry towards the bedside

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Tissue engineering (TE) combines biomaterials, cells and bioactive molecules to design functional constructs or drug delivery systems capable to restore or improve tissue/organ functionality. The proper design of scaffolds that provides the structural and mechanical support to the regeneration process or drug delivery systems that allow a localized and controlled payload release are key aspects to stimulate and guide the repair and formation of a new functional tissue. In this scenario, polyurethane (PU) biomaterials could represent a valuable alternative to commercially available natural and synthetic polymers, as their high chemical versatility could be exploited to design polymers with conveniently tuned physico-chemical properties to meet TE strict demands. The high potential of PUs in the biomedical field also lies in their high workability that makes it possible to fabricate PU constructs via both conventional and advanced techniques. In this contribution, the previously mentioned PU high chemical versatility has been exploited to design both thermosensitive gels and thermoplastic materials. A wide family of thermoplastic PUs has been synthesized starting from poly(ϵ -caprolactone) diol, an aliphatic diisocyanate and different chain extenders (e.g., aliphatic cyclic diols, amino-acid derived diols or diamines), demonstrating that a fine tuning of PU physico-chemical and biological properties can be obtained by simply changing a single building block [1]. These PUs have been processed by thermally induced phase separation, fused deposition modelling and electrospinning for soft TE (cardiac, muscle and tendon TE). Poly(ester ether urethane)s have been also synthesized at different PCL/poly(ethylene oxide) (PEO) w/w ratios to design NPs for the release of hydrophobic and hydrophilic chemotherapeutics. Moreover, building blocks containing BOC-protected amino groups have been exploited to functionalize the designed materials with bioactive molecules (e.g., peptides, proteins) following the removal of the amine protecting group in mild acid conditions. Additionally, PUs can be easily surface functionalized by plasma treatment for acrylic acid grafting/polymerization followed by protein grafting via carbodiimide chemistry. Amphiphilic PUs which aqueous solutions with proper concentrations are able to undergo a temperature-driven sol-to-gel transition have been also designed starting from the PEO-poly(propylene oxide)-PEO triblock copolymer Poloxamer 407 (P407) [2]. Injectable thermosensitive polymers able to gel in physiological conditions within few minutes and with improved mechanical properties and residence time in aqueous environment compared to P407-based gels (used as control) have been optimized and their high potential in the release of drugs/therapeutic ions in a sustained and controlled way has been thoroughly demonstrated. Novel thermo- and photo-sensitive PU-based sol-gel systems and PU-based supramolecular hydrogels are currently under investigation as bioinks in bioprinting and self-repairing thixotropic gels for drug delivery, respectively. The proper exploitation of PU high versatility could thus lead in the future to the fabrication of the optimal scaffolds/drug release systems for the treatment and repair of almost all tissues of the human body. Hence, polymers that belong to the wide family of PUs could realistically open the way to a new era in the biomedical field, thanks to the possibility to synthesize ad-hoc designed materials suitable to a variety of processing technologies for advanced biomedical applications.

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Dynamic rheological characterisation of silicones for podiatry applications

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This work shows an effective methodology to evaluate the static and dynamic viscoelastic behaviour of two different silicones for a possible application in podiatry. The aim of this study is to compare their viscoelastic properties according to the different stress conditions upon which they can be presumably subjected when used in podiatry orthotic applications. Indeed, in the selection of suitable materials for this application, it should be taken into account that an orthoses can be subjected to a set of static and dynamic shear and compressive forces. For this purpose, this study proposed an effective methodology to this aim. Two commercial silicones (Blanda-Blanda and Master) were studied, respectively used as a “soft” and a “hard” silicone in podiatric applications. Cylindric samples were prepared from the raw silicone with a commercially available curing agent (Reaktol). In order to mimic a realistic scenario, three kinds of rheological tests have been considered: shear stress sweep, compression frequency sweep and shear frequency sweep. All of these tests have been carried out with simultaneous control of the static force at three different levels. The static force represents a static load similar to that produced by the weight of a human body on a shoe insole. Figure 1 reports the results of the compression frequency stress test, obtained applying a periodically oscillating stress under different static load values from 0 to about 90 kPa. This test allowed for measuring the values of storage and loss modulus. The overall proposed experimental methodology can provide very insightful information for better selecting suitable materials in podiatry applications. This study focuses on the rheological characterization to choose the right silicone for each podiatric application, taking into account the dynamic viscoelastic requirements associated to the physical activity of user. Accordingly, one soft and one hard silicones of common use in podiatry were tested. Each of the two silicones exhibited not only different moduli values, but also, a different kind of dependence of the dynamic moduli with respect to the static load.

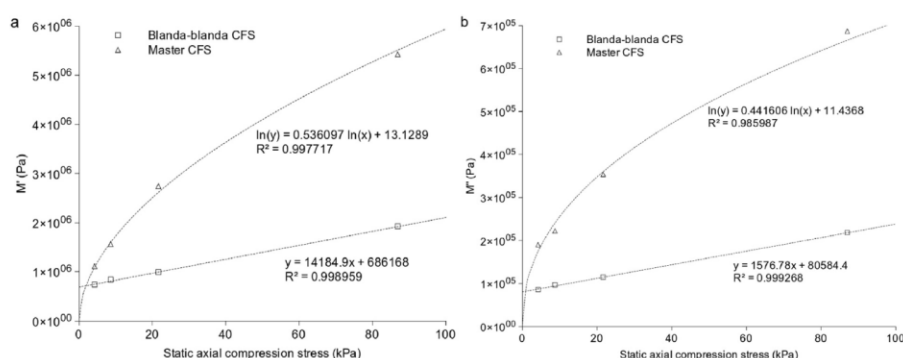


Figure 1. Longitudinal storage (a) and loss (b) module of the Blanda-Blanda and Master silicones in compression frequency stress tests at 1 Hz as a function of static applied load.

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Super strong enzymes. Polysulfides as sacrificial stealth components of protein conjugates

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A number of protein therapeutics have achieved great clinical success, ranging from antibodies to growth factors, to enzyme replacement therapies, e.g. for lysosomal storage diseases. Most often their performance is severely hampered by instability during storage (freeze-drying and transport), immune recognition (removal from circulation) and/or degradation by proteolysis or oxidation [1]. Classically, with considerable degree of commercial success, poly(ethylene glycol)(PEG) has been conjugated to proteins to greatly enhance circulation times of proteins, yet PEG provides solely a steric barrier and is associated with significant therapeutic limitations, such as reduced activity of protein/enzymes upon conjugation, immunogenicity and advanced blood clearance upon repeated injection (indeed, this has led to the removal of PEG-uricase from the market) [2]. Here, we have developed a new class of polymer, poly(thioglycidyl glycerol)(PTGG), that endows enhanced stability of protein-conjugates to freeze-drying, proteolysis, opsonisation and oxidizing conditions. PTGG contains a thioether backbone (conferring antioxidant properties) and a glycerol side-group (conferring water solubility and cryo/lyoprotection). The cytotoxicity profile was found to be similar to PEG (i.e. non-toxic), with an even lower capacity of complement activation. To conjugate PTGG to a protein, it is first reacted with the maleimide of a difunctional linker, and then grafted (via activated esters) to lysine residues of lysozyme which was used as a model enzyme. The conjugate had an activity comparable to that of the native enzyme but was significantly less recognized by anti-lysozyme antibodies (90% reduction) and above all showed greatly enhanced resistance to a panel of proteases (pepsin, trypsin, chymotrypsin, carboxypeptidases Y and B) as well as aggressive oxidants such OH radicals, hypochlorite and peroxyxynitrite. Additionally, the conjugates activity was almost unaffected by 10 freeze-drying cycles, whereas PEGylated and native enzymes were reduced to ~30% of their original activity. In summary, PTGG displays significantly improved properties over the current gold standard (PEG) for polymer-protein conjugates in every aspect evaluated thus highlighting its significant potential for use with therapeutic proteins/enzymes, particularly those required to function under highly oxidising conditions (e.g. for lysosomal storage diseases).

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How side reactions can influence poly(2-oxazoline) synthesis for polymer therapeutics and hydrogels

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Poly(2-oxazolines) (PAOx) are an interesting class of polymers for *e.g.* polymer therapeutics and hydrogels. By incorporating the correct 2-oxazoline comonomers a wide variety of linear and branched/network polymers can be realized with a tailored structure. A challenge remains the exact distribution of the functional comonomer units and branching points over the copolymer chains, taking into account chain-to-chain deviations and side reactions.

In the present contribution [1-3], it is illustrated that the combination of advanced kinetic Monte Carlo modeling and experimental analysis allows (i) the detailed assessment of the relevance of side reactions such as chain transfer and macropropagation; and (ii) an unbiased ranking of functional copolymers in view of their functionalization degree.

Model-based design is successfully performed to identify the optimal chemical structure of the reactants and synthesis conditions to maximize the functionality degree, both for low and high average chain length polymers (Figure 1). The developed platform is generic and can thus be applied for a wide range of functionalization chemistries, including reversible deactivation radical polymerization (RDRP).

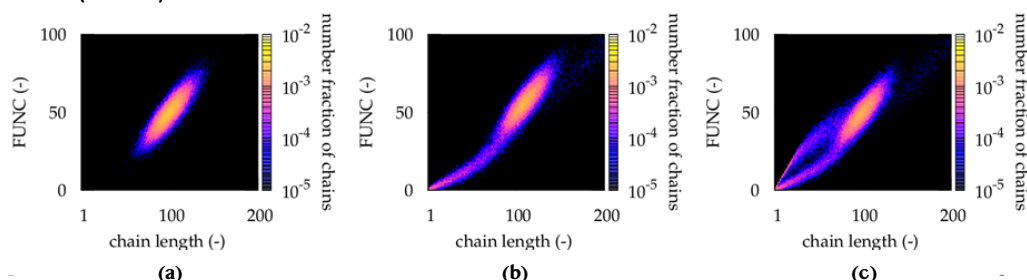


Figure 1. Impact of side reactions on functionality – chain length distribution (FUNC-CLD) under equimolar conditions (total monomer concentration: 3 mol L⁻¹; solvent acetonitrile; target DP of 100; 140 °C; overall monomer conversion of 100%); (a) formally no chain transfer; (b) with chain transfer but formally without chain initiation of the formed oxazolinium fragment; (c) with chain transfer and the latter chain initiation.

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Investigation of the physical behaviour of multifunctional polymer composites with thermal energy storage/release capability

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Thermal energy storage (TES) consists in storing excess heat and releasing it where/when needed, filling thus the gap between thermal energy demand and supply [1,2]. Organic phase change materials (PCMs), like paraffin waxes, poly(ethylene glycol), and fatty acids, are particularly effective in accumulating/releasing latent thermal energy, as they are able to store large quantities of heat per unit mass in a narrow temperature range, with limited volume variations [3,4]. The drawback of the PCM leakage above the melting temperature can be overcome by encapsulating PCMs in polymeric or inorganic shells, by embedding them in a polymer network or by confining them in porous carbonaceous or inorganic structures, forming thus a shape-stabilized PCM. If shape stabilization is performed with a thermally conductive structure, i.e. a carbonaceous nanofiller, the problem of the low thermal conductivity of PCMs can also be overcome [5,6].

TES systems based on PCMs find applications in several fields, i.e. in building constructions to enhance indoor thermal comfort and reduce energy demand for heating and cooling, in photovoltaic panels for solar thermal energy storage, in the development of smart thermo-regulating and technical garments, or into electronic devices to avoid overheating. In most of these applications, TES systems are only juxtaposed to the main structure as an additional component. However, it would be interesting to embed TES capability directly into the structural mass of the component, thus obtaining a multifunctional structure. In this sense, polymer composites appear to be particularly suitable, since they can be composed of various phases and are easily tailorable to multifunctionality. Up to now, little has been done to investigate the possibility of designing and fabricating such structural TES composites and to characterize their mechanical and thermal properties [1,6].

The aim of the experimental work of our research group was that to investigate the possibility to develop multifunctional polymer composites with thermal energy storage/release capability, to be utilized for several technological applications. Structural and semi-structural epoxy/carbon fiber composites with TES capability were prepared by adding both shape stabilized paraffin and paraffin microcapsules, and the role of the obtained microstructure on the physical properties of the prepared materials was highlighted. Also thermoplastic polymer composites were developed both by using long and short reinforcing fibers, and the effect of the melt compounding process on the TES capability of these materials was investigated. Thermoplastic polyurethane (TPU)/microcapsules blends, to be applied in winter sports applications, were also prepared, and the possibility to process these materials with innovative technological processes (i.e. fused deposition modelling) was assessed.

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Poly(hydroxyalkanoate)s (PHAs) architectures by ring-opening polymerization of functional β -lactones

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Poly(hydroxyalkanoate)s (PHAs) are a class of natural or synthetic aliphatic polyesters which feature the same three-carbon backbone structure, only differing by their substituent (R) in β -position.

PHAs have attracted considerable interest as “green” engineering plastics. These biodegradable and biocompatible polymers represent a targeted choice for in particular packaging, and biomedical applications in tissue engineering and as drug delivery systems [1].

Recent highlights of research at Rennes University in the field of 1) tunable catalytic systems for the ring-opening (co)polymerization (ROP) of β -lactones (e.g. β -butyrolactone (BL; R = Me), benzyl β -malolactonate (MLA^{Bn}; R = CO₂CH₂Ph),...) into their corresponding PHAs (poly(3-hydroxybutyrate) (PHB), poly(benzyl β -malolactonate) (PMLA^{Bn}),... respectively), and 2) original sequence controlled PHAs featuring a high degree of control over molecular and microstructural characteristics, will be presented. This process is catalyzed by an yttrium complex stabilized by a nonchiral tetradentate amino alkoxy bisphenolate ligand {ONOO^{R'2}}²⁻, which features both a good activity and a high degree of control over the molar masses of the resulting functional poly(3-hydroxyalkanoate)s [2-6]. Our most significant achievements in this endeavor include the development of strategies that enable the synthesis of alternated PHA-based copolymers, and the evidence of the relationship between the chemical structure/composition of the macromolecules.

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D-, L-arginine derived polyamidoamino acids and sodium deoxycholate: the importance of self-assembly in chiral recognition

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Chiral synthetic polymers have widespread applications, from stereoselective synthesis to chiral recognition. Chiral centers, either in the main chain or as side pendants, allow polymers to self-assemble into ordered conformations [1], due to their structure-directing power. Recently, a new class of chiral polymers emerged, named polyamidoamino acids (PAACs). ARGO7 isomers, the first synthesized polymers, were obtained in water by stepwise polyaddition of L-,D- or D,L-arginine to N,N'-methylenabisacrylamide (Figure 1) [2]. These polymers maintained the chirality of the parent aminoacids and proved capable to self-organize into pH dependent conformations [3]. L-ARGO7 resulted highly citobiocompatible [2] and preferentially localize in the perinuclear region of Balb/3T3 cells. It remains to be ascertained whether any chiral interactions may arise with other biological components, as well. To assess chiral recognition, sodium deoxycholate (NaDC), one of the components of bile salts, was chosen as a chiral model surface. Through a stepwise mechanism, NaDC is able to form chiral micelles, whose self-assembly behaviour is affected by pH, concentration and ionic strength. Pulsed-gradient spin echo NMR (PGSE-NMR), circular dichroism (CD), dynamic light scattering (DLS) and zeta potential (ZP) emphasised the complex equilibria behind chiral recognition. In particular, NaDC showed three main pH dependent behaviour: homogeneous solution, gel phase, flocculation and aggregation. All of them are characterised by different CD patterns. ARGO7 isomers proved able to chirally and/or electrostatically interact with all the different NaDC conformations. Evidence of chiral recognition was detected in NaDC gel phase by means of CD spectroscopy. Both D- and L-ARGO7 led to changes in shape and magnitude of CD patterns, whereas D,L-ARGO7 did not modify the CD spectra of NaDC. Incoming SANS studies will probably highlight the mechanisms and dynamics of these polyelectrolyte-micelle systems.

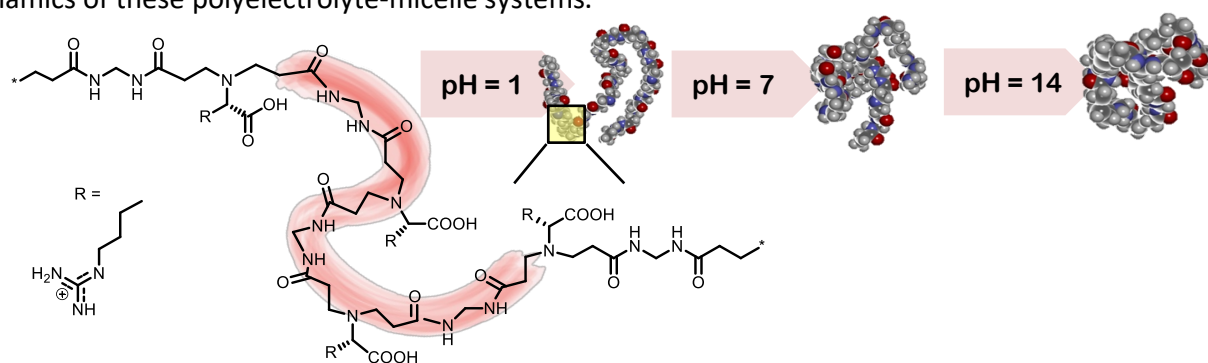


Figure 1. ARGO7 repeating unit and pH dependent structures from molecular dynamics simulation [3].

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Unique trafficking to the cell cytosol and to the nucleus of a luminescent linear polyamidoamine-ruthenium complex

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Nanomedicine holds great promises to change the way drugs are delivered to their target, owing to the use of nano-sized drug carriers capable to enter cells and be trafficked intracellularly via energy dependent pathways [1,2]. This is very different from the way most drugs arrive to their target, often based simply on their solubility and partition coefficients in lipids and water. Despite some valuable successes, drug delivery remains rather challenging and several factors are still limiting its potential. Among such factors, it has emerged, for instance, that most nano-sized carriers entering cells via endocytosis are later trafficked along the endolysosomal pathway to the lysosomes, where the low pH and abundant proteases can degrade and destroy the internalised cargo. Strategies to escape the endosomes and lysosomes are being investigated. For instance, for gene therapy and other therapies based on the delivery of DNA several viral and non-viral vectors have been investigated to try to deliver the genetic material to the cell nucleus or cytosol [3]. Cationic polymers are often used for this purpose [4] because of their capacity to complex the negatively charged DNA or RNA molecules while also showing to be capable to promote endosomal escape. Among the many polymer species employed as gene delivery vectors, linear polyamidoamines (PAAs) are very interesting and promising materials.

In this communication it will be presented a new polycationic PAA endowed with a luminescent Ru complex (PhenAN-Ru) and its ability to target the cell nucleus. It shows unique trafficking to the cell nucleus of all the treated cells, also at polymer doses as low as cytotoxicity is very low, and the supposed mechanism for entering cells will be discussed.

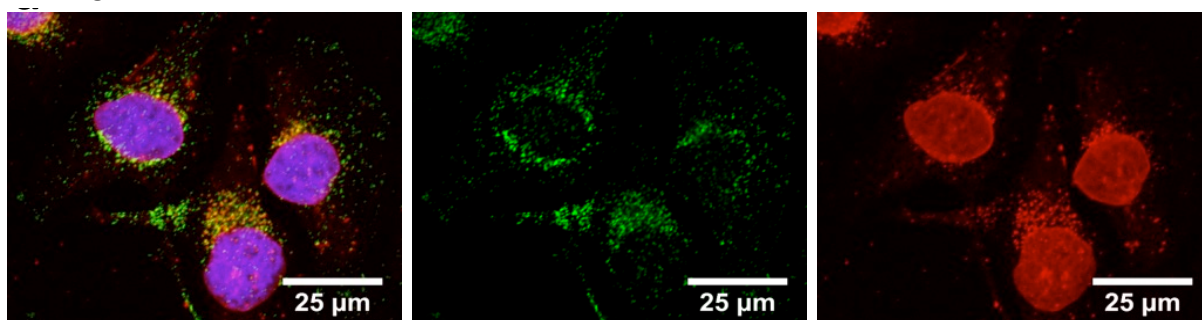


Figure 1. Confocal fluorescence images of HeLa cells after 24 h exposure to PhenAN-Ru (30 µg/mL), showing accumulation of the polymer (red) in nucleus as well as in the lysosomes (LAMP-1 staining, green).

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IUPAC 100 years serving chemistry

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2019 celebrates the 100 years since the foundation of IUPAC, and the 150 years since the discovery of the Periodic Table of the Elements by Mendeleev. The role and relevance of IUPAC in the promotion of a sustainable chemistry in the XXI century and the planned events will be highlighted.

Chemical and physical functionalization of nanogels for controlled intracellular drug release

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Nanogels are promising nanotools for intracellular delivery of therapeutics molecules to counteract central nervous system (CNS) disorders [1]. However, loading nanocarriers with hydrophilic drugs presents the main drawback of undesired rapid diffusion, which in turn reduces pharmacological activity at the target site. To overcome this aspect, chemical or physical functionalization strategies can be pursued. Here, we report the synthesis of nanogel systems for controlled intracellular drug release following two routes: the former based on the formation of chemical bonds between the drug and the nanogel through a thiol-sensitive linker (hereinafter “NGC”), and the latter based on the generation of ionic interactions between the drug and the polymeric network (hereinafter “NGP”). NGC nanodevices were based on polyethylene glycol (PEG) linked to rhodamine (RhB, used here as a drug mimetic) through a disulfide bond, and polyethyleneimine (PEI) labelled with Cy5 dye for nanogel traceability. The selectivity of drug delivery was due to the disulfide bond that can be disrupted intracellularly by glutathione or cysteines present in the cytosol. Given the key role of microglia in modulating CNS inflammation, nanogels were tested in combination with microglia cultures. Fluorescence colocalization studies showed that nanogels were internalized by target cells, and that the drug mimetic was selectively released in the cytosol after 4 days (Figure 1A) [2]. NGP nanodevices exploited the different protonation degree of PEI as a function of pH, giving rise to uncharged or positively charged nanogels. The resulting tunable drug-nanogel electrostatic interaction successfully modulated the cargo release *in vitro* (Figure 1B), avoiding any questionable chemical modification of the drug [3].

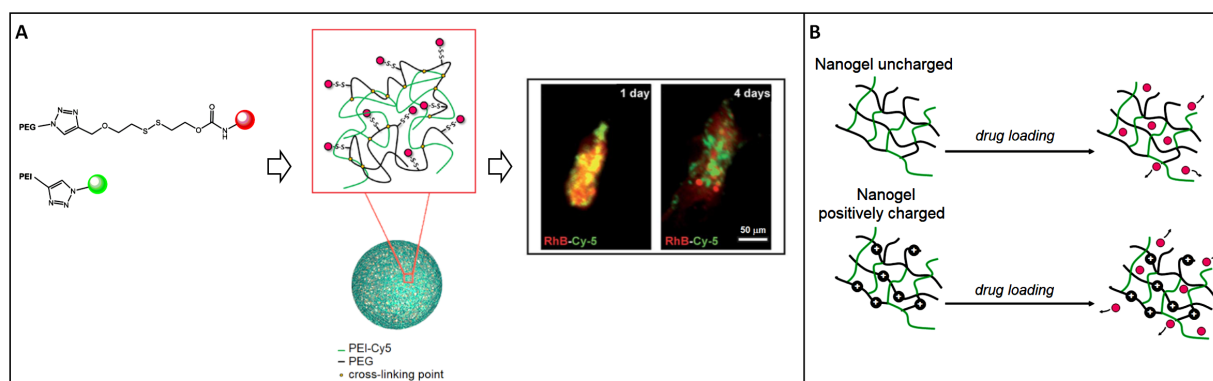


Figure 1. A: scheme of functionalized nanogels NGC with RhB (red dot) and Cy5 (green dot) and corresponding fluorescence delocalization in microglia, after 4 days. B: Scheme of uncharged and positively charged NGP for drug release modulated by electrostatic interactions

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From artificial to natural-derived electroactive hydrogels: materials for soft actuation, microfluidics, biotechnology

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Electroactive hydrogels (EAHs) are soft hydrophilic polymeric materials able to change their shape in response to an applied electrical stimulus in aqueous environments [1]. Due to the co-presence of both fixed and mobile ions inside their polymeric matrix, they can convert electric energy into soft motion in a reversible and controllable way. They are of strategic importance for the development of remotely controlled soft underwater actuators for applications in soft robotics, fluidics and microfluidics, biomedicine and biotechnology [2-5]. Our group synthesized a novel EAH as a copolymer of 2-hydroxyethylmethacrylate, acrylonitrile and Na-4-vinylbenzenesulfonate, obtained through a UV radical polymerization. We studied its swelling in different aqueous solutions, its mechanical properties and electro-mechanical actuation, showing its responsiveness at low applied potentials ($< 1V$) and in biological media [6]. We also embedded a low amount of cellulose nanocrystals inside the gel to improve its properties and we prototyped a smart fluidic component demonstrator integrating multiple actuators able to cooperatively bend together [7]. Then we synthesized a more biocompatible EAH using cellulose derivatives as the main components. Its properties are investigated and then we shaped many samples as natural algae and we assessed how their motion can be controlled with electric signals to mimic natural seaweeds movements under the effect of water flow, a first step towards the development of hybrid habitats where artificial smart algae could cohabit with real living organisms or microorganisms.

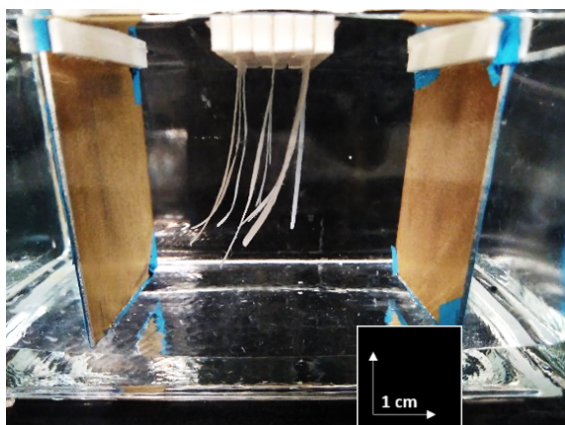


Figure 1.

Three arrays of the cellulose-based electroactive hydrogels, placed between a couple of flat electrodes to apply the desired potential.

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Novel formulations based on polylactic acid for biomedical applications

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Poly(lactic acid) (PLA) is one of the most widely applied polymers in the biomedical field for its peculiar features, such as biocompatibility, biodegradability and processability, which properties fulfill the complex needs of this application [1]. Nevertheless, some specific issues have to be considered for its exploitation, that is the hydrophobicity, the low impact toughness, the lack of function groups as well as the difficult degradation tuning [2]. In our works, we focused on new types of applications of PLA in the biomedical field and on strategies for overcoming the polymer drawbacks.

In particular, a novel composite system, suitable to be used as drug carrier and based on stereocomplex PLA and chitosan (CHI), have been developed by the assembly of enantiomeric poly(lactide)s onto the surface of CHI microparticles, taking advantage of their cation-dipole interactions. For this purpose, *ad hoc* low molecular mass poly(L-lactic acid) (PLLA) and poly(D-lactic acid) (PDLA) were synthesized by ring-opening polymerization (ROP) of L- and D-lactides. The microparticles, which were prepared by using a bead generator, were modified by the Layer by Layer (LbL) deposition of up to three PDLA/PLLA bilayers. The drug, namely procaine, was loaded in the CHI microparticles for release behavior characterization. Compared with the uncoated microparticles, procaine release from stereocomplex-coated microparticles decreased, showing a reduction in the burst phenomenon. These results reveal that the presence of the stereocomplex multilayer, decreasing the porosity of the developed system, acts as a barrier for the procaine diffusion and they represent a starting point for future studies aimed at developing anesthetic release systems [3].

In another study, the application of PLA-based composite films, which were made conductive by dispersing graphite into the polymer matrix, as electro-stimulated drug delivery systems was reported. Indeed, graphite nanoplatelets allowed to improve the material features, such as thermal, mechanical and electrical properties and, from the other, promoted the homogeneous dispersion of the drug in the polymer film. This study was based on the application of a porphyrin as drug model molecule, whose interactions with the surface of the filler were also found to improve, in turn, the dispersion/exfoliation of graphite nanoplatelets in the system. The proper dispersion of high-aspect-ratio nanoplatelets corresponded to the formation of an electrically percolating network, resulting in a high electrical conductivity of the composite. Furthermore, it was demonstrated that the porphyrin release could be viably improved/tuned through the application of an electrical voltage to the composite film. That is, thanks to the exploitation of the synergy between graphite and a π -stacking-forming-molecule, such as porphyrin, we were able to develop, for the first time, an electrically-controlled release system based on PLA [4].

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Liquid crystalline polymers for regenerative medicine and tissue repair

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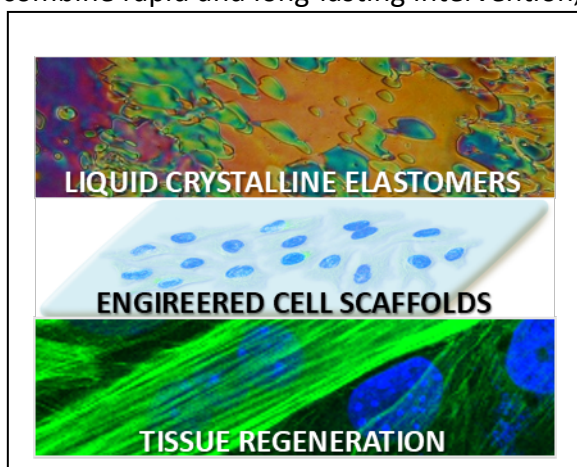
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The extraordinary features of Liquid Crystalline Elastomers (LCEs) make them great candidate to address unsolved tissue engineering issues, opening for the preparation of complex cell scaffolds for cell culturing and artificial tissues [1]. Preliminary assessments of the material biocompatibility were performed on Human Dermal Fibroblasts (HDF), murine muscle cells (C2C12), and, more interestingly, for culturing human induced pluripotent stem cell-derived cardiomyocytes, proving them capable to develop adult-like dimensions and a more mature cell function in a short period of culture in respect to standard supports [2]. Furthermore, the LC alignment inside the materials was demonstrated able to control cellular organization in myoblast culture, with an observed cellular alignment corresponding to the nematic director inside the material [3]. On the other hand, advanced materials able to work as actuators for the treatment of muscle injuries, could combine rapid and long-lasting intervention, which is the main goal in regenerative medicine. LCEs



could result in a good advancement also in this field since, once stimulated, they can mimic muscle force production. A palette of biocompatible LCEs was prepared and precisely characterized in terms of passive and active mechanical properties, showing improved muscle-like characteristic. Combination of the demonstrated biocompatibility and suitability as cell scaffolds with the muscle like mechanics could open for new solutions in tissue repair and regeneration.

Figure 1. POM of an LCE; cartoon representing cells on an engineered scaffold, and differentiated C2C12 cells on a LCE.

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2D hybrid substrates for functional polymer-based materials

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Polymer nanocomposites (PNC) with 2D nanostructured fillers (i.e., layered silicates, layered double hydroxides, graphene etc.) have emerged in the past decades as a promising class of materials with improved mechanical, thermal and barrier performance [1]. Final material properties depend not only on the size of particles but also on the properties of the interphase and interfacial interactions, which govern the matrix chain mobility, filler dispersion and distribution [2]. Much work has been done on the modification of both filler and matrix in order to tune and optimize the reciprocal interactions and to create a co-continuous organic/inorganic phase necessary for improving the thermo-mechanical properties.

Recently, in addition to the optimization of PNC structural features, emphasis is given to the introduction of new functional properties (i.e. optical, electrical, sensing, bioactive, etc.) by dispersing 2D hybrid heterostructures, used as “nanocarriers” of specific active moieties [3]. In particular, the 2D structure of layered double hydroxides (LDHs) can accommodate functional organic molecules (i.e. dyes, biomolecules, oligomers, stabilizers, etc.), which are firmly anchored by anionic bond to the layer surfaces. These hybrid host-guest systems can be used as fillers for polymers thus obtaining PNC where the structural properties are ruled by the organic/inorganic polymer network, and the functional properties are related to the chemical nature of the substances incorporated into the filler. In this way, PNC can be endowed with interesting optical, sensing and bioactive properties by simply transferring the targeted property from the 2D hybrid system to the polymer matrix through the nanocomposite preparation.

This lecture reviews the results obtained in our laboratory about the preparation of PNC obtained by dispersing 2D hybrid materials modified with functional molecules, such as dyes, antioxidant and antibacterial agents [4-7] for possible packaging and sensor applications. The role of the 2D substrate functionalization and of the chemistry at the interface for the optimization of morphology and final properties of PNC will be discussed.

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Polymers with aggregation-induced emission: a land of opportunities

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From sensing to lighting, fluorescence is one of the most studied photophysical processes due to the variety of its possible applications. It was found that sensing based on fluorescence is one of the most powerful method for the detection of analytes with high sensitivity and selectivity thanks to the tailored design of the emitting probes. Notably, light emission in the solid state is essential for practical utility, thus enabling the diffusion of fluorophores with excellent emission also in the aggregate state [1,2]. Recently, the dispersion of luminescent aggregachromic dyes into polymer films have been effectively used for the preparation of materials showing optical response to visible light. The basic principle of these chromogenic materials is founded on colour changes in absorption or in emission associated with the structural modifications of the molecular assemblies of dyes dispersed in the polymer phase. Chromogenic materials can respond to various stimuli (for example, thermal, mechanical, or chemical solicitations) through a macroscopic output in which the energy of the stimulus is properly transduced into optical variations [3,4]. Fluorescence also plays a pivotal role in solar collectors called also luminescent solar concentrators (LSCs) [5,6]. In LSCs, sunlight penetrates the top surface of an inexpensive plastic or glass waveguide. This light is absorbed by luminescent molecules which are either embedded in the waveguide or applied in a separate layer on top or bottom of the waveguide. A fraction of the re-emitted light is trapped in the waveguide by total internal reflection and then collected at the edges of the device to produce electric power by means of photovoltaic cells even with a cloudy sky. In this technology, fluorophore features are fundamental in solar harvesting. Therefore, a proper design of the emitter characteristic has a pivotal role. In this contribution, the most illustrative examples developed in our group of fluorescent polymers in sensing and solar harvesting are provided and discussed with the reference of the recent literature.

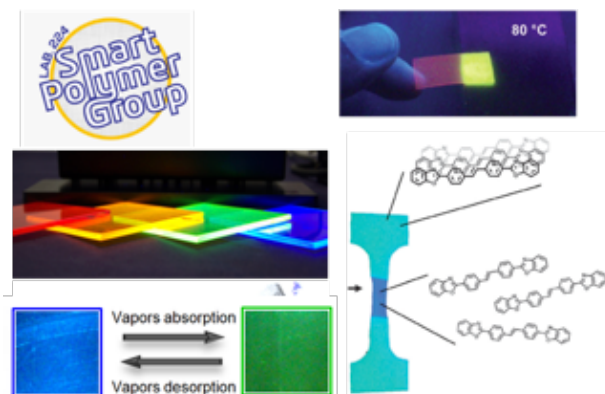


Figure 1. Examples of polymers with aggregation-induced characteristics developed in the lab.

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The use of biopolymers for siRNA and antisense intracellular delivery

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Many protein toxins have evolved to access a variety of relatively inaccessible intracellular compartments. Counted among this number are proteins such as ricin toxin, shiga toxin, diphtheria toxin and anthrax toxin. These proteins display diverse architecture ranging from AB₅ to AB configurations and depending upon the specific B chain in question, entertain a number of strategies from direct membrane penetration to utilizing retrograde trafficking pathways to access a plethora of intracellular compartments including the cytosol. Typically, the A chain will exhibit catalytic activity proportional to both cellular intoxication and virulence. However, given the facile nature of protein recombination, attenuation is relatively simple. Here we describe the ability of attenuated anthrax toxin (ATx) to manipulate endocytic cargo sorting for the purposes of drug delivery, traversing intracellular compartmental boundaries for nucleic acid delivery. We report not only the efficiency with which siRNA and antisense effectors are delivered but also the mechanisms they utilize to traverse the barriers responsible for intracellular compartmentalization. Attenuated Atx:ASO complexes had transfection efficiency approximately equivalent to Nucleofection. In HeLa cells, at 200 pmol ASO expression of the target gene was $5.4 \pm 2.0\%$ relative to an untreated control after 24 h. Using 200 pmol ASOs, Nucleofection® reduced Synt5 expression to $8.1 \pm 2.1\%$ after 24 h. PA:LFn-GAL4:ASO transfection of non- or terminally-differentiated THP-1 cells and Vero cells resulted in $35.2 \pm 19.1\%$, $36.4 \pm 1.8\%$ and $22.9 \pm 6.9\%$ (respectively) target gene expression after treatment with 200 pmol of ASO and demonstrated versatility. Nucleofection with Stealth siRNA™ siRNA reduced HeLa Synt5 levels to $4.6 \pm 6.1\%$ whereas treatment with the PA:LFn-PKR:siRNA resulted in $8.5 \pm 3.4\%$ Synt5 expression after 24 h (HeLa cells). These data underscore the tractability of this approach to both antisense and siRNA delivery. Further, we also continue to explore the possibility of utilising biologically derived supramolecular systems for drug delivery in the form of siRNA-loaded exosomes.

Bioprintable hyaluronic acid-based hydrogels for 3D *in vitro* studies

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The 3D bioprinting technology represents a transformative approach that revolutionized the way of think medical and pharmaceutical research areas [1]. During the last 10 years, it has been used to fabricate living tissues, thanks to CAD-based software, that convert images acquired through a 3D scanner into files readable by bioprinters. This technology has various applications, in particular in regenerative medicine, one of the greatest interdisciplinary challenges, aiming to trigger the biological regeneration of failed human tissues and organs [2]. In addition to tissue engineering, 3D cell printed structures have also been used as research models for drug screening and cancer research; indeed, 3D cell cultures more adequately simulate the natural 3D cell environment, thus furnishing more physiologically relevant information and more predictive data for *in vivo* tests [3].

Natural polymers are generally chosen to design hydrogels, since they offer the advantage to mimic the native extracellular matrix (ECM). Hyaluronic Acid (HA), a component of the ECM, represents an ideal material for 3D cell culture applications, thanks to the interaction with cell surface receptors like CD44 and RHAMM (hyaluronan mediated motility receptors), that are strongly involved in the regulation of cell adhesion, spreading and differentiation [4].

In the context of the preparation of new hyaluronic acid-based hybrids hydrogels with the aim to furnish a viable cell model to be applied in 3D *in vitro* studies, herein we present the preparation and the chemical-physical characterization of modified hyaluronic acid.

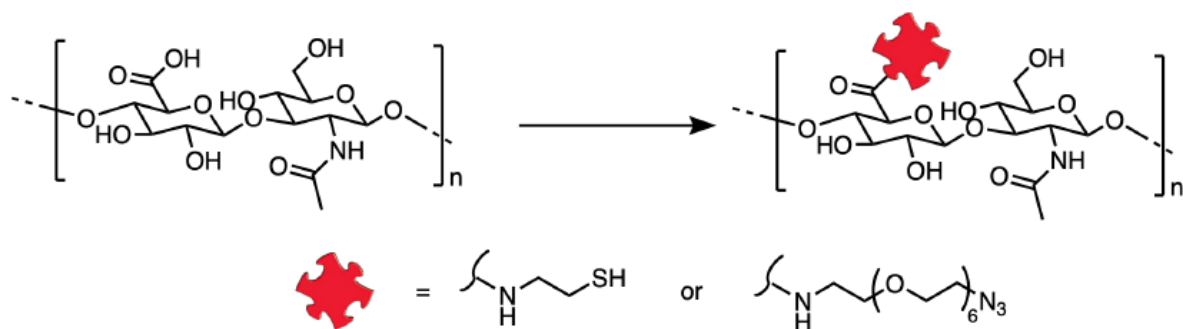


Figure 1. Hyaluronic acid functionalization.

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Three dimensional biomimetic hydrogel to deliver factors secreted by human mesenchymal stem cells in spinal cord injury

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Stem cell therapy with human mesenchymal stem cells (hMSCs) represents a promising strategy in spinal cord injury (SCI) [1,2]. However, both systemic and parenchymal hMSCs administrations show significant drawbacks as a limited number and viability of stem cells in situ. Moreover, cell therapy delivered systemically (intravenous injections) could lead to a limited efficacy due to the unfeasibility of the cells to cross the blood brain barrier [2]. In this study, we evaluate a new agarose/carbomer based hydrogel that combines different strategies to optimize hMSCs viability, density and delivery of paracrine factors. The three-dimensional polymeric networks chosen correspond to a library of chemical nanostructured hydrogels, highly tunable in terms of molecular structure and biocompatibility [3]. In addition, we combined RGD tripeptide and 3D extracellular matrix deposition to increase the capacity to attach and maintain healthy hMSCs within the hydrogel over time. In order to optimize and evaluate the hMSCs adhesion and viability several hydrogel compositions and different loading protocols were developed and tested [4]. We first seeded hMSCs into HG RGD and we measured the ECM deposited over time. A progressive ECM deposition was observed from 1 up to 14 days, where ECM deposition reaches a “plateau”. Thus, for a second hMSCs seeding, we decided to deposit ECM up to 14 days and then we lyophilized the HG RGD + ECM to allow a new encapsulation of hMSCs by a sponge-like loading. This hydrogel with ECM is able to maintain hMSCs viable for a longer period and to maintain their stemness during time.

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Detection of single block impurities in ab block-copolymers by gel permeation chromatography and ultra high performance liquid chromatography

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Research surrounding block copolymers has been increasing rapidly since the 1980s, as their ability to form complex ordered systems has led to applications in many fields including drug delivery and advanced materials (thermoplastic elastomers) [1,2]. Single block contaminants may occur during synthesis due to various causes such as poor initiation during chain extension of the A block or undesired exogenous initiation of the B block. These impurities are often difficult to identify by bulk techniques such as nuclear magnetic resonance. Gel permeation chromatography (GPC) has been embedded in polymer research and the industry for decades now [3]. The technique is used as the primary tool to determine molecular weight and molecular weight distribution of polymer samples. Addition of in-line light scattering detectors and viscometer led to the implementation of triple-detection GPC. The new improved and user-friendly OMNISEC multi-detector GPC system from Malvern Panalytical with its highly sensitive light-scattering and Refractive Index (RI) detectors, can provide excellent measurements of several materials. GPC has also been advanced by the Waters Acquity Advanced Polymer Characterisation (APC) system with the introduction of ultra-high performance liquid chromatography (UPLC™), allowing the high-resolution and high-speed GPC analyses of materials [4]. The powerful OMNISEC advanced multi-detector system, and specifically the OMNISEC Reveal multi-detector module, has been combined with the UPLC™ system from Waters making it possible to analyse polymers by advanced GPC with improved resolution, reduced sample concentrations, solvent usage and run times. Using multi-detection, a variety of polymer parameters are characterised in a single measurement. Two of these parameters, molecular weight and intrinsic viscosity, are used to generate Mark-Houwink plots, which can be used to identify chemical and structural differences between polymer samples. Often the detection of impurities in block copolymers is solely based on molecular weight increase and retention peak symmetry. However, this relies on the assumption that the lower molecular weight region is not a block copolymer without any further characterisation. To ratify this, the power of triple-detection GPC on the OMNISEC system has been used to construct Mark-Houwink plots, which make it possible to differentiate between AB block copolymer and a single block impurity. Additionally, the combination of the UPLC™ system from Waters and the OMNISEC Reveal multi-detector module allowed to conduct separation and characterisation of these block copolymers to identify impurities with dramatically increased efficiency.

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The influence of fillers and nucleating agents on polypropylene crystallization at high supercooling measured by Fast DSC

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Fillers and additives can be classified into inactive nucleating agents, that have no significant influence on the crystallization kinetics, and active nucleating agents, that accelerate the crystallization process. The active nucleating agents can be further classified in particulate additives and additives which self-assemble the structure which accelerates crystallization.

On the example of polypropylene (PP) the nucleating activity is measured in a wide temperature range (between 0 °C and 130 °C) using Fast Differential Scanning Calorimetry (FDSC), the recently introduced Flash DSC 2+.

The influence of sorbitol-type nucleating agents, different carbon-nanotubes, calcium carbonate and nano-diamonds of the isothermal and non-isothermal crystallization kinetics is analyzed. As a result, it could be shown that all additives of investigation influence the crystallization process of PP. Furthermore, it is shown that all additives (also calcium carbonate) accelerates the crystallization process in a dedicated temperature range. Outside of this range the nucleating agents are not active.

The measurements have been shown further that especially the measurement of the isothermal crystallization process is very sensitive for the characterization of the nucleating activity of an additive.

Structure, dynamics and barrier performance relationship in furan-based polyesters

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World plastic production has reached impressive values and is going to further increase in the coming years [1]. Indeed, plastics cover up to 50% of primary food packaging, thanks to their low price, lightness, easiness of production and processability, modulation of properties and durability. This massive consumption is accompanied by a consistent waste generation, mainly disposed in landfills [1], with very high carbon footprint. In order to reduce environmental impact, the use of bioplastics can be considered as a sustainable alternative to traditional fossil-based plastics. The great and growing interest in sustainability is so driving the development of biobased materials, i.e. obtainable from renewable sources, which could be or not biodegradable and that are characterized by minimum waste production, transport efficiency and controlled after-use disposal and/or recycling, being this last considered by European Commission the best option [2]. In the particular case of food packaging application, high barrier properties and proper mechanical response are fundamental requisites, and not many biopolymers could be employed for this scope. Conversely, the most used commercial products are multilayer and formed by different materials, preventing thus the recycling of the product. In this context, polyesters synthesized from 2,5-furan dicarboxylic acid can be considered very interesting candidates since combine biobased nature with outstanding barrier properties and very good mechanical behavior. Such characteristics render them particularly promising as monomaterials for food packaging applications, in view of their possible recycling.

In the present work, poly(pentamethylene furanoate) PPeF (Figure 1) a new furan-based polyester, has been synthesized and characterized. Despite being an amorphous and rubbery polymer at room temperature, PPeF can be processed in form of film. This last shows exceptional barrier and mechanical response in view of an application in flexible food packaging. With the aim of shedding light on the origin of solid-state properties of this polymer, a study combining calorimetric, diffractometric and spectroscopic techniques has been carried out.

The results obtained evidenced the formation of a particular microstructure, different from the classical crystalline phase, that could be responsible for the final properties of this new smart bioplastic.

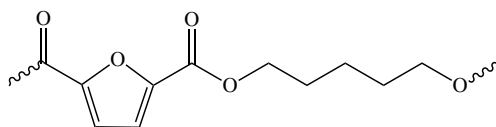


Figure 1. Poly(pentamethylene furanoate) chemical structure.

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Balancing hydrophobic and electrostatic interactions in thermosensitive polyplexes for nucleic acid delivery

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Introducing multiple functionalities, like cationic and thermosensitive properties, in a polymer design has acquired attention to improve the efficacy of nucleic acid delivery. Complete condensation of the nucleic acids and the formation of stable complexes are crucial for achieving effective intracellular delivery. Therefore, in this study the balance between hydrophobic and electrostatic interactions has been investigated for thermosensitive plasmid DNA (pDNA)-loaded polyplexes. NPD triblock copolymers consisting of a thermosensitive *N*-isopropylacrylamide (PNIPAM, N), a hydrophilic poly(ethylene glycol) (PEG, P) and a cationic 2-(dimethylamino)ethyl methacrylate (PDMAEMA, D) block with different block lengths were prepared using a hetero-functional PEG macroinitiator [1]. In this study it is shown that there is a critical balance between the electrostatic and hydrophobic interactions between the multifunctional polymer and pDNA at temperatures above the CP. If the length of the cationic block and the N/P ratio are high enough, the electrostatic interactions between the pDNA and the cationic block of the polymer are superior over the hydrophobic thermosensitive interactions, resulting in sustaining the polyplex nanostructure. These results provide new insights into the design of polymers for advanced drug delivery systems, such as polyplex-releasing thermosensitive hydrogel systems for the controlled and local delivery of nucleic acids [2].

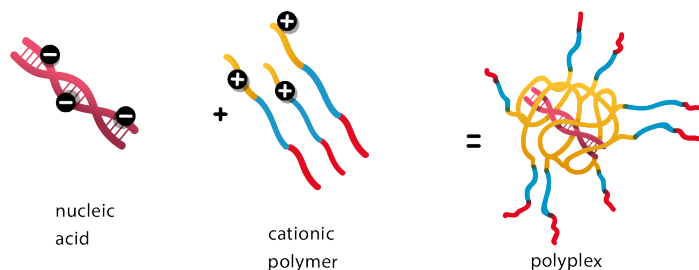


Figure 1. Schematic overview of polyplex formation using triblock copolymers (cationic block in yellow, uncharged hydrophilic block in blue and thermosensitive block in red).

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Formation of an interpenetrating polymer network of polyurea and silicone rubber in the vacuum casting process

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The use of silicone casting molds in the vacuum casting process for the replication of prototypes made of polyurethane is state of the art. With this method, the gap in plastics processing between very small quantities (rapid prototyping) and very large quantities (injection molding) might someday be closed. The development of a versatile, economical small-batch production process has enormous advantages for the future of plastics processing and the everyday handling of plastic products. For vacuum casting a silicone mold based on a master form is filled with a curing two component polyurethane resin. For the possible application in small-batch production, the output of the casting molds is decisive for economic efficiency. However, according to the current state of the art, the tools fail due to aging of the silicone rubber even after a few casting cycles. It has been shown that the aging of the tools is due to the diffusion of a polyurethane resin component. During the casting process, isocyanate diffuses into the silicone surface where it reacts with residual moisture to form urea derivatives, which quickly leads to hardening of the silicone matrix and failure of the mold. In this work we present an in-depth investigation of the chemical and physical mechanisms of the diffusion and aging process. Thermal measurements such as differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) as well as spectroscopic techniques such as X-ray photoelectron spectroscopy (XPS) and infrared spectroscopy (FTIR) have been used to verify urea formation within the silicone matrix. The use of a helium-ion microscope (HIM) and an atomic force microscope (AFM) enabled the visualization of an arising interpenetrating polymer network from polyurea and silicone rubber.

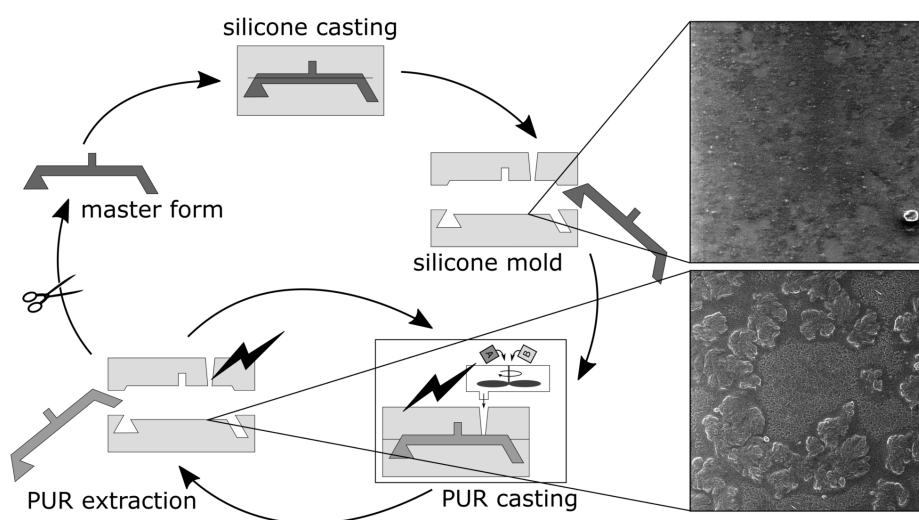


Figure 1. Schematic representation of the vacuum casting process and HIM imaging of the silicone surfaces.

Smart polymeric carriers tailored towards biotechnological applications

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Rational design of functional polymers based on natural or synthetic polymers paved the way to develop smart carries with diverse morphological shapes and sizes. Such smart carries displayed great potential in many biotechnological applications such as carriers for drug delivery, nanoreactors for enzymatic reactions and functional coatings. Polymersomes is one of the promising caries which obtained by the self-assembly of amphiphilic copolymers. The potential of polymersomes lies in their ability to load both hydrophilic and hydrophobic cargo. Thereby our interest is directed to establish shape persistence polymersomes with tunable membrane permeability that is cable to control the diffusion of their cargo depending on external stimuli. Particularly, we have developed a shape persistence polymersomes based on photo crosslinkable pH sensitive block copolymers. Stable polymersomes over the whole pH range were feasible after short UV irradiation time. Furthermore they show impressive reversible swelling-shrinking behaviour upon switching between acidic and basic pH. Such on-off switches have been conducted to traffic the diffusion of different cargo from and to polymersomes. Indeed, polymersomes decorated with folic acid on their surface and loaded with chemotherapy agent in their lumen displayed significant selectivity towards tumour cells compared to the normal cells [1].

In other direction, we developed polymersomes to be used as smart nanoreactor. In details, host-guest interactions between adamantane and β -cyclodextrin as well as the tunable membrane permeability of polymersomes have been used to control a sequential docking and un-docking processes of small molecules and nanometer-sized protein on the inner and outer spheres of the polymersome membrane. To achieve this goal polymersomes decorated with adamantane groups were prepared. Regarding the gust molecules, cyclodextrin conjugated with rhodamine was used as model for small molecules. However, stained hyperperanched polymer conjugated to cyclodextrin was used as model for macromolecules. Interestingly, the inner and the outer spheres of polymersome membrane were selectively decorated with different functional groups depending on the molecular weight and charge of the guest molecules [2].

Additionally, polymersomes loaded with antiseptic compound have been used for surface modification of urinary catheter to prevent biofilm formation. This was achieved by using polymersomes functionalized with free amine groups that can react with a polydopamine coated silicone catheter through Schiff base formation.

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Chitosan-coated colloidal lignin particles as novel stabilizers for Pickering emulsion

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Amphiphilic colloidal lignin particles (CLPs) can be utilized as stabilizers for oil/water Pickering emulsions. However, unmodified CLPs are not well suited to stabilization of vegetable oil-based Pickering emulsions that break into biphasic systems with broad size distribution of oil droplets [1]. To overcome this problem, we studied coating of CLPs with a thin film layer of chitosan by simple physical adsorption. At a constant 1:1 volume ratio of olive oil to aqueous chitosan-coated CLP (chi-CLP) suspension, the formed Pickering emulsion showed a transition from biphasic to monophasic droplet distribution when the mass ratio of chitosan to CLP was above 50 mg/g. At a fixed coating ratio of 50 mg/g, the average size of the oil droplets decreased with increasing concentration of chi-CLP suspension. At 1 wt% chi-CLP suspension, the resulting Pickering emulsion showed the smallest mean oil droplet size of $\sim 17\ \mu\text{m}$ with a uniform distribution. The positively charged chi-CLP layer locating at the interface of oil/water could be ionically cross-linked by sodium triphosphate (TPP), which resulted in enhanced mechanical stability of the Pickering emulsion that retained their capsule morphology after drying and rewetting.

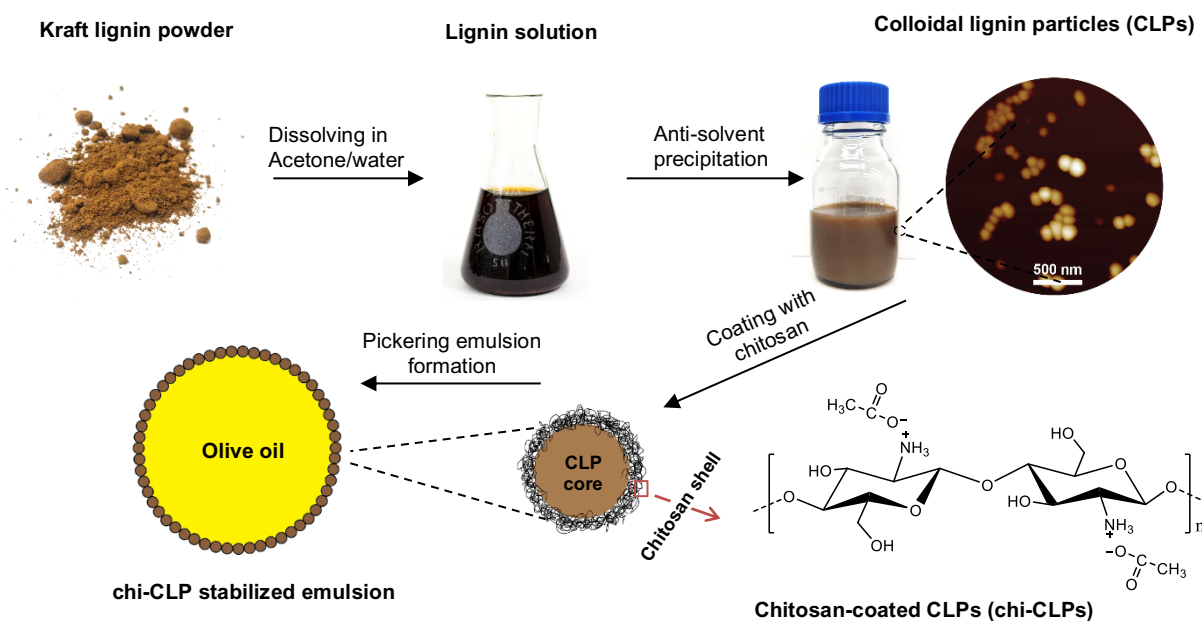


Figure 1. Route of Pickering emulsion formation with chitosan-coated lignin particles.

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POSTER PRESENTATIONS

Cell response to polymeric scaffolds with tunable macro-microstructural features prepared by additive manufacturing

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Additive Manufacturing (AM) techniques are based on a computer-aided design and manufacturing process for layer upon layer fabrication of a 3D object with a high degree of reproducibility and an advanced control over pore size, geometry and distribution, as well as external shape and size [1]. In biomedical application AM techniques represents a powerful tool for the development of scaffolds with tailored key features that can act on cell response and bioactivity [2]. In fact, recent evidence suggests that scaffolds micro- and nanostructural features affect cell adhesion, spreading, growth, propagation and reorganization [1]. Scaffolds based on Poly(methyl methacrylate) (PMMA), develop as permanent implants endowed with a porous structure to favour their integration with the surrounding tissues, were prepared by two different AM techniques namely fused deposition modelling (FDM) and computer aided wet spinning (CAWS). Cell response to the developed scaffolds was investigated through a careful *in vitro* biological evaluation employing the murine embryo fibroblast cell line Balb/3T3 Clone A31 [3]. Quantitative evaluation of cell proliferation onto the two typologies of PMMA scaffolds indicated their suitability to sustain a good proliferation, highlighting interesting differences that could be correlated to the different structure of the scaffolds. Visualization of cell adhesion and morphology, performed by confocal laser scanning microscopy and scanning electron microscopy, confirmed the quantitative data.

Scaffolds based poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) (PHBHHx) polymer, investigated as a biodegradable material for biomedical application that support osteogenesis, were prepared by CAWS employing different solvent/non-solvent ratio (90:10, 80:20, 70:30 and 60:40% v/v) that allowed for obtaining scaffolds with different porosity and mechanical properties. Quantitative and qualitative biological evaluation, carried out employing MC3T3-E1 preosteoblast cell line on PHBHHx selected scaffolds, highlighted significant differences in cell response that could be correlated to the morphological differences present in the various types of sample.

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Drug-loaded polymeric nanoparticles functionalized with an MMP-cleavable peptide for glioblastoma treatment

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Glioblastoma (GBM) is the most common and aggressive brain tumor characterized by a poor response to standard therapies. The presence of the blood brain barrier (BBB) at the peripheral regions of the tumor limits the amount of chemotherapeutic drugs that can reach GBM [1]. Recently, the use of engineered polymer nanocarriers combined with radiotherapy has been proposed to overcome these limitations [2]. Radiation can trigger the overexpression of matrix metalloproteinases (MMP), a family of proteolytic enzymes which are able to enhance BBB permeability, thus allowing nanoparticles with size > 100 nm to accumulate into the tumor, while limiting the damage to healthy tissues.

In this work, new engineered polymeric nanoparticles (NPs) were developed to penetrate GBM tumors and selectively release a chemotherapeutic agent, in order to treat GBM effectively. Biocompatible and biodegradable Poly(lactic-co-glycolic acid) (PLGA) - poly(ethylene glycol) (PEG) nanoparticles, loaded with doxorubicin (DOXO) were functionalized with a targeting peptide (Figure1). In particular, an Activable Low Molecular Weight Protamine (ALMWP)-based peptide was selected for conjugation because it can be activated only where MMPs are overexpressed, such as in GBM cells. NPs activity was preliminarily evaluated *in vitro*. The tests confirmed that the overexpression of MMPs by the tumor cells enhance nanoparticles internalization and the cytotoxicity of the encapsulated DOXO.

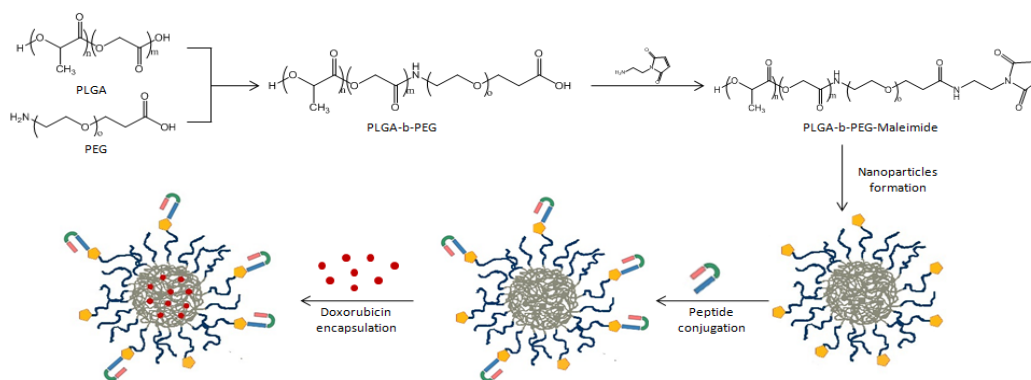


Figure 1. Schematic representation of synthesis of polymeric NPs.

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Polymeric nanoparticles as diagnostic tools in type I diabetes regenerative therapy

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Diabetes is one of the most hard and challenging diseases for modern medicine research and iNanoBIT [1] project focuses on the development of a new medical device for β cells and islet Transplantation.

Aim of the project is the development of a bioartificial pancreas (BAP) for islet / cell transplantation in Diabetes type I. In this context new multimodal imaging techniques will be developed taking advantage of smart functionalized nanoparticles, obtained from poly glutamic acid (PGA), a biodegradable anionic homopolyamide and Chitosan, a linear polysaccharide by BBS's assembly protocol. In detail, nanoparticles were functionalized with recognition motifs to target β cells and imaging molecules to assess cells functionality. Different functionalization was assessed using: a) recognition motifs of β cells receptors; b) a chelator agent that allow NMR, PET and SPECT analysis; c) NIR dye to develop a new optoacoustic diagnostic protocol (MSOT). Here we will present, nanoparticles design synthesis and functionalization with preliminary biological data.

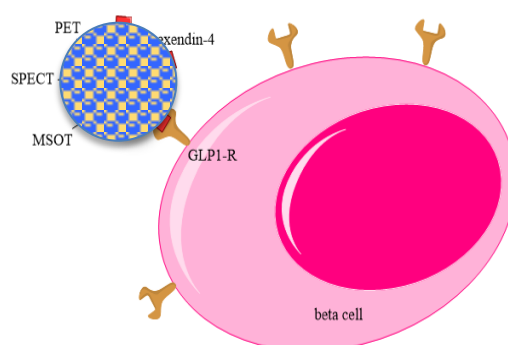


Figure 1. Polymeric nanoparticle and its identification on the β cell.

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Acknowledgments

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Amphiphilic triblock copolymers for combined therapy

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Polymeric nanoparticles (NPs) play an important role in drug delivery as nanocarriers for small hydrophobic molecule drugs and as non-viral vectors for gene delivery [1] (plasmid DNA or siRNA). Combination of both properties in a single nanoparticle formulation can be useful in cancer treatment. In this topic, amphiphilic autoassembling block copolymers for realization of NPs offer a wide range of opportunities, due to the possibility of fine tuning the structure (nature, length and ratio of blocks) and surface properties of final NPs. In this work, synthesis and characterization of amphiphilic triblock copolymers based on poly(ethylene glycol) (PEG)-poly(dimethylaminoethyl-methacrylate) (pDMAEMA)-polycaprolactone (PCL) with different blocks length are described, with the aim to realize NPs for a combined anticancer therapy. The structure of triblock copolymers is shown in Figure 1.

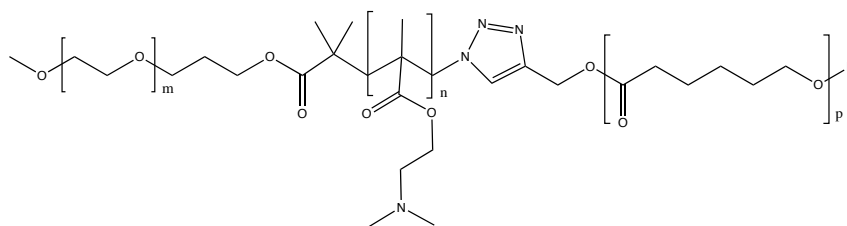


Figure 1. Structure of triblock copolymers.

PEG was chosen as hydrophilic block for its stealth properties; pDMAEMA cationic block, intended for siRNA complexation, was synthesized via atom transfer radical polymerization (ATRP) [2]; finally, PCL was conjugated via “click” reaction through copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) as biodegradable hydrophobic block. Copolymers were characterized through ¹H-NMR, FTIR, GPC and DSC. NPs were obtained by nanoprecipitation and characterized for size, polydispersity index, surface charge and stability. Critical micellar concentrations (CMC) were determined. NPs were loaded with docetaxel (DTX), and a non-targeting pool siRNA was adsorbed by gentle stirring on DTX-loaded NPs. The complexes were characterized by electrophoresis on agarose gel. The final NPs showed narrow size distribution and good loading efficiency and release profiles.

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***De Novo* generation of a streamlined reporter system for monitoring the modulation of gene expression**

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Reporting a modulation of gene expression is crucial for testing target specificity and efficacy of potential drugs based upon siRNA, antisense oligonucleotides and gene editing technologies. Here a rapid, reliable and cheap reporter system has been developed to accelerate and simplify this process using mammalian cells grown in culture. This reporter system relies on Human Embryonic Kidney (HEK)293 cells stably expressing green fluorescent protein (GFP), fused-in-frame to LacZ and bicistronically expressed with red fluorescent protein (RFP). The LacZ gene encodes β -galactosidase (β -gal), which can hydrolyze synthetic X-gal from a colorless precursor to a bright blue compound that is spectrophotometrically detected at 620 nm. The single mRNA that encodes these proteins can be targeted, and modulation efficiency can be determined by measuring X-gal conversion in relation to cell number *i.e.* total cell protein. To develop this assay, the cell line was characterized by microscopy, the transgene sequenced and the expressed proteins detected by western immunoblotting. X-gal conversion was monitored over time and normalized to total cell protein concentration. Finally, β -gal activity was expended relative to untreated cells. When anti-GFP siRNA was loaded into HeLa derived exosomes, β -gal activity was $16.8 \pm (\text{SEM}) 0.5 \%$ ($n=3$; $P= 0.0026$) of the control after 48h. Further, $16.8 \pm (\text{SEM}) 0.7 \%$ ($n=3$; $P= < 0.0001$) of β -gal activity was documented after 72h. When ASOs specific for RFP were loaded into exosomes and incubated with HEK293 cells, $51.0\% \pm 11.2$ (SEM; $n=6$; $P < 0.0001$) β -gal activity was documented. Nucleofection of the aforementioned siRNA and ASOs also gave significant knockdown. Nucleofection with 200 pMol of anti-RFP ASO resulted in $19.1 \pm 3.6 \%$ control β -gal activity over 72h. Nucleofection with 70nM anti-GFP siRNA resulted in $19.9 \pm 6.3\%$ β -gal activity after 48h. This reporter system has shown tractability over a 48-72 time scale when a variety of transfection methodologies are used to target with RFP or GFP coding genes.

Collagen polymer's shell on Halloysite nanotubes overcoming burst of drug release and local toxicity

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Scientific literature shows many examples of an efficient application of Halloysite nanotubes (HNTs) in drug delivery. Taking advantage of cylindrically-shaped crystal form of the HNT and its hollow empty lumen, above-mentioned nanoparticle can be filled with a variety of therapeutics [1]. However, the following drug release profile demonstrates great drug liberation in the first minutes just after immersion of Halloysite based nanoconstructs in the medium, followed by sustained drug release. The above-mentioned burst of initial release is called *dose dumping effect*. It has a severe impact on stability of drug-Halloysite based nanoconstructs, resulting in an uncontrollable drug liberation before reaching the targeted site. In addition, *dose dumping effect* entails unexpected local toxicity. Herein, we propose Halloysite nanotubes grafting with multi-functional collagen coating. This biocompatible and bioresorbable polymer shell acts as a layer that covers Halloysite nanotubes and blocks the entrances of the Halloysite hollow tube, entrapping the drug immobilized in HNTs, until nanoconstructs reach the suffering organ. More to the point, the coating is removable as a consequence of response to the pH- and enzyme-stimuli. The proposed collagen coating has another exceptional feature: it is able to selectively target wounds, fibrotic tissues and finally tumour cells, since it is recognized by several receptors of pathological cells [2]. In the present work we implemented innovative technique for HNTs and collagen shell visualization using 3D multiphoton microscopy [3]. While kinetics of drug release was studied by LC-Mass analysis.

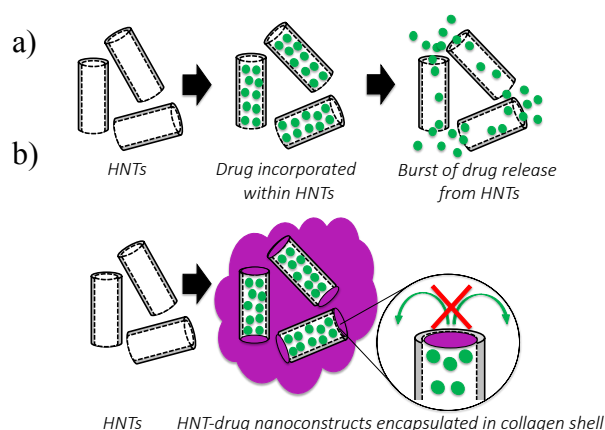


Figure 1. Schematic illustration of burst of drug release from HNTs (a); Overcoming burst of drug release by incorporating HNT-drug nanoconstruct in collagen shell (b).

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Design of polymeric biomimetic structures and interfaces through nanotechnology

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Biomimetic structures aim to reproduce the morphology and composition of the physiological environment, providing cells with the cues and stimuli necessary for their proliferation and/or differentiation. So far, nanotechnology has been used as a versatile tool to develop new advanced and patient-specific therapies [1]. E.g., the electrospinning technique allows to fabricate nanofibrous membranes with three-dimensional (3D) architectures from a variety of materials, either synthetic, biological, or composites [2]. In this work, the demonstrated proofs of concept for two different applications of the processing of polymeric materials through nanotechnology in advanced clinical applications are illustrated: (1) the realisation of a 3D exocrine glandular tissue model to reproduce in vitro the physiological architecture of the physiological gland, and (2) the development of a multicomponent mesh device for abdominal wall hernias. The 3D exocrine glandular model aims at reproducing the acinar-ductal morphology and the composition of the pancreatic gland, overcoming the limitations of the current models. Melt electrospinning was used to create a fibrous matrix reproducing the glandular structures, obtaining a controlled porosity and a more complex geometry [3]. Then, the obtained geometry will be combined with cells (i.e., acinar and ductal progenitor cells) (Figure 1a). A commercial polypropylene surgical mesh applied in the regeneration of damaged abdominal tissues was coated with a nanostructured multi-layered structure (Figure 1b) to i) guarantee suitable mechanical support; ii) promote muscle tissue growth and repair; iii) prevent adhesion between the mesh and abdominal viscera, and iv) attenuate the host inflammatory response. Polycaprolactone fibres provide the mesh with reinforcement properties, whereas gelatin fibres will stimulate cell attachment and proliferation [4].

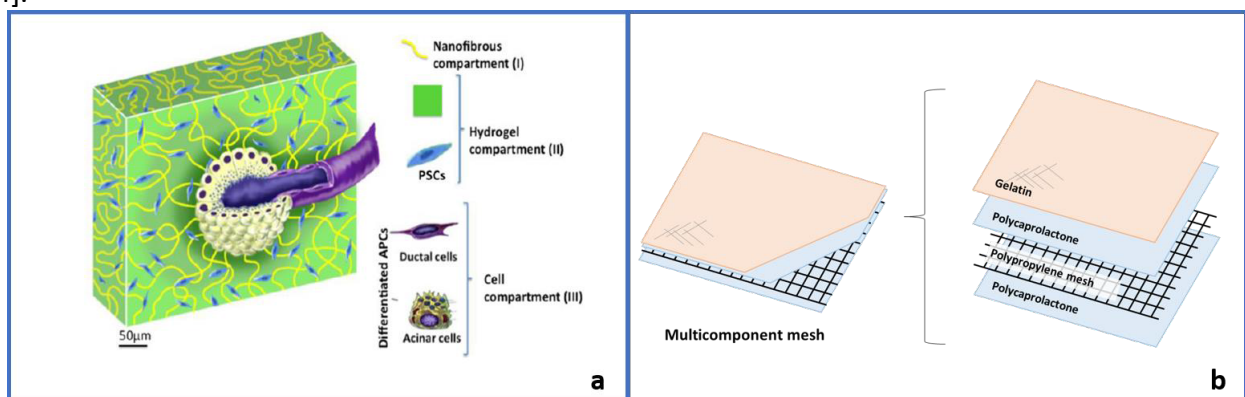


Figure 1. Applications of biomimetic structures: a) 3D model of Exocrine Pancreatic functional unit; b) multicomponent device for abdominal wall hernia surgery.

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Biodegradable electrospun PBS/keratin blend scaffolds for tissue engineering applications

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One of the main challenges of tissue engineering is the development of three-dimensional matrices able to support cells adhesion and proliferation. Among the polymeric materials used for tissue engineering applications, polylactic acid (PLA), polyglycolic acid (PGA), polycaprolactone (PCL) and their copolymers are the most common. Another aliphatic polyester, recently approved by the Food and Drug Administration, that is emerging thanks to its thermal stability, high melting temperature and, most importantly, its biocompatibility, is poly(butylene succinate) (PBS) (Figure 1a) [1]. Unfortunately, nevertheless biocompatible, it is characterized by a low cell affinity, which represents the main limit to an extensive use of PBS in regenerative medicine applications. On the other hand, natural biopolymers like keratin proteins (Figure 1b), that can be obtained from hair, nails, feathers and wool, are characterized by high biodegradability and biocompatibility, thanks to the presence of tripeptides Arg-Gly-Asp (RGD) and Leu-Asp-Val (LDV) motifs in its primary structure. Unluckily, the low molecular weight and poor mechanical properties, typical of keratin, make this material difficult to handle and process [2]. In order to overcome the main drawbacks of both PBS and keratin, keeping at the same time their positive features, in the present work PBS/keratin biodegradable nanofibrous membranes were prepared by electrospinning a blend solution of the two polymers. As it is well known, through this easy and versatile technique it is possible to obtain fibres with nanometric diameter through the application of a high voltage electrostatic field between a needle of a syringe, in which the polymeric solution is disposed, and a grounded metallic collector. Electrospun fibrous membranes are characterized by high surface/volume ratio, high porosity and fibre interconnectivity, which make them particularly suitable for cell adhesion, growth and proliferation, as their structure mimics that of natural extracellular matrix (ECM). The so-obtained membranes were characterized from the molecular, thermal, morphological and mechanical point of view. In addition, in the perspective of tissue engineering applications, the degradation rate in enzymatic environment and fibroblasts proliferation were also evaluated. The results obtained so far are encouraging: in fact, keratin becomes processable and the mechanical properties of the scaffold obtained from the PBS/keratin blend are significantly improved compared to keratin scaffold, the fragility of this latter being consistently reduced.

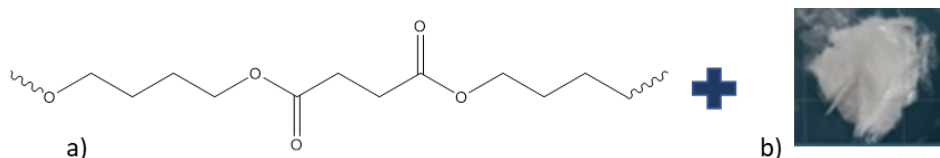


Figure 1. Chemical structure of PBS (a) and keratin powder (b).

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Functionalized biopolymers for 3D cell models and tissue engineering applications

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The native Extracellular Matrix (ECM) is a dynamic and hierarchically organized microenvironment secreted by cells in the space between them, with a crucial role in both normal and disease processes. This intricate network is characterized by a wide variety of polysaccharides, proteins and glycidic-based motifs that goes from glycosaminoglycans (GAGs) and proteoglycans (PGs) to glycoproteins and glycolipids. This milieu is dynamically degraded and remodelled by cells during their biological functions. In the last decades the development of regenerative medicine was in charge of the design of biomaterials because of their capability to mimic the complex ECM microenvironment and their utility in different field, such as drug screening, cell biology studies and tissue engineering. Here different biopolymers have been obtained and formulated using different chemoselective methodologies. Polymers with different degrees of modification have been characterized in term of biomolecular and biological properties to assess new 3D in vitro models [1].

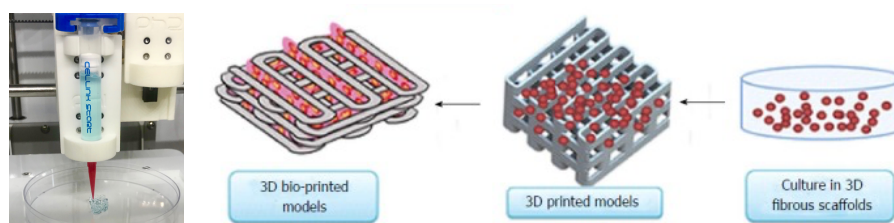


Figure 1. Schematic representation of 3D culture studies.

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Ministero della Salute, RICERCA FINALIZZATA 2016 RF-2016-0236294 (1/3/2018-28/2/2021) Theory enhancing Projects. Title: Dissecting the link between pulmonary stromal changes and lung cancer progression for biomarkers discovery and therapeutic intervention.

Elastin-based hybrid hydrogels as ECM mimics in 3D cell culture and tissue engineering applications

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Hydrogel-based biomaterials are considered of wide interest because they have several features suitable to encapsulate cells, such as high-water content, swellability, and permeability, which facilitate transport and diffusion of essential nutrients, oxygen, and waste across the scaffold [1]. Thus, carefully designed hydrogels have the potential to offer mechanical support, chemical properties and biochemical cues that lead to cellular function in a native manner.

This attractive concept can be exploited for two different research applications: the use of 3D cell-cultures in drug screening and cancer research [2], since it is widely accepted that 3D cell cultures more adequately simulate the natural cell environment, and tissue engineering, in response to the clinical demand for tissue or organ repair and replacement, leading to the development of regenerative medicine field, one of the greatest visionary challenge of the last decades [3]. These hydrogels applications can be even expanded by the advent of 3D printing or 3D bioprinting technology which allow to deposit them in a precise and controlled way and fabricate the complex architecture of tissues as well as mini-tissues and organ-on-a-chip models [4].

Aim of the work is the development of new 3D printable model for cell cultures and cancer research. Proteinaceous and polysaccharidic polymers have been functionalized and used to produced hydrogel with tunable stiffness. The produced hydrogel will be used for cell encapsulation and 3D bioprinting procedure.

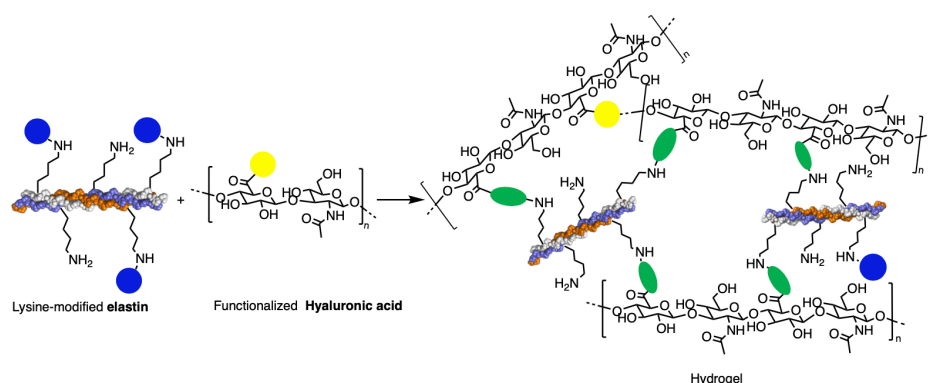


Figure 1. Schematic representation of hydrogel formation via click reactions between biorthogonal functional groups.

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Preparation and characterization of electroactive polyaniline polymers for biomedical applications

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The aim of this work is to produce a new type of highly conducting polymer for biomedical applications. Polyaniline (PANI) films, with different concentrations (10, 25, and 40 wt%) of aniline hydrochloride monomer, were produced by *in situ* polymerization at ambient temperature in the presence of polyvinyl alcohol (PVA). The films obtained from the blends were characterized to determine their structural morphology, thermal, electrical, and mechanical properties. The SEM images revealed a heterogeneous distribution of conductive PANI particles in the continuous PVA matrix. FTIR spectra showed shift of peaks at 3220 cm⁻¹ and 1420 cm⁻¹ from higher wavelength to a lower wavelength, indicating an increase of PANI concentration in the blends. The electrical conductivity of the blend films showed an increase from 10⁻⁸ to 10⁻³ S/cm. The major degradation peak of TGA thermogram showed significant elevation with increase in PANI concentration indicating improvement in stability. The stress-strain values of the PANI blend decreased substantially with increasing PANI concentration. Future implication of this project is the possible use of polyaniline fibers as artificial muscles.

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Thermosensitive hydrogels loaded with hemoderivatives: promising platforms for sustained release of growth factors to favor tissue regeneration

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In recent years, platelet-rich plasma (PRP) and platelet lysate (PL) have emerged as promising autologous biological treatment modality for the use in regenerative medicine (tissue regeneration and healing capabilities). Indeed, PRP and PL comprise hundreds of bioactive proteins, including growth factors (i.e. platelet derived growth factor (PDGF), vascular endothelial growth factor, and epithelial growth factor), peptides, and cytokines that stimulate healing of skin and soft tissues. Apart from favoring tissue healing, PRP and PL also stimulate angiogenesis and decrease pain and swelling. Moreover, they do not present any problems associated with immunogenicity [1]. PRP is a high concentration of platelets derived from whole blood isolated by centrifugation to separate and concentrate platelet-containing plasma from red blood cells. On the hand, PL is a protein extract obtained from the fractionation of platelet concentrate by physical and chemical means.

Here, preliminary thermosensitive hydrogel-based formulations were developed for the local sustained delivery of PRP and PL. The formulations were designed with the aim to improve the release of PRP and PL for favoring the regeneration of tissues after surgical operation [2]. The novel hydrogels were based on Pluronic F127, multiblock co-polymers that undergo a sol-gel transition near physiological temperature and pH. Different type of formulations were tuned changing several excipients to obtain a slow and prolonged release of PRP and PL, lasting at least 7 days. All the hydrogels were characterized measuring viscosity and sol-gel transition temperature by rheological analysis. *In vitro* release assays were performed to evaluate the release profile of the growth factors contained in PRP and PL. The quantitative determination of them was carried out by ELISA test.

The hydrogels obtained have potential applications for PRP and PL delivery. Moreover, they can act as filler materials and depots for other bioactive molecules to improve tissue regeneration and healing.

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Integrin-targeted polyamidoamine (PAA) nanodroplets for paclitaxel delivery

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Integrins are cell-adhesion molecules overexpressed on tumour cell membranes. They could represent specific biomarkers to rationally design targeted nanomedicines, allowing selectivity between tumour and normal cells. Arginine-glycine-aspartic (RGD) peptides that bind to specific integrins have been widely used to provide ligand-mediated targeting capabilities to nanocarriers. Various nanoparticles containing RGD moieties that could be actively target toward integrins have been explored [1]. Polyamidoamines (PAAs) are well-known, hydrophilic, biodegradable and biocompatible polymers suitable for several biotechnological applications. Among these, a peptidomimetic PAA, designed to mimic RGD peptide, was previously synthesized [2].

The aim of this work was the development of RGD-mimic-PAA shelled theranostic nanodroplets to achieve selective tumour targeting of paclitaxel.

Nanodroplets, spherical core/shell nanostructures filled by vaporizable compounds (i.e. perfluorocarbons) with sizes in the nanometer order of magnitude, are versatile multifunctional nanocarriers for the delivery of anticancer drugs [3]. They have been proposed as multifunctional theranostic platform with the capability to provide US imaging and drug delivery [4].

Nanodroplets (NDs) were formulated using decafluoropentane for the core and AGMA 1, a guanidine-substituted peptidomimetic PAA, for the shell [2]. Paclitaxel-loaded NDs were prepared dissolving the drug in the decafluoropentane core. Fluorescent NDs were obtained loading 6-coumarin in the core as fluorescent marker. Blank and paclitaxel-loaded ND formulations were *in vitro* characterized determining size, surface charge, drug loading, morphology and drug release studies. The viscosity and the shell shear modulus of NDs were determined through Discovery HR1 Hybrid Rheometer. Echogenic properties of ND formulations were demonstrated by ultrasound ecography imaging. For *in vitro* biocompatibility evaluation, the cytotoxicity of NDs was determined on melanoma cell lines by MTT assay. Moreover, the internalization of fluorescent NDs was studied by confocal microscopy.

AGMA1-shelled NDs with sizes of about 300 nm and positive surface charge were obtained. They were able to load paclitaxel with a good encapsulation efficiency and release it with a prolonged release kinetics. Integrin-targeted PAA NDs could represent a promising theranostic tool for the targeted delivery of paclitaxel.

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Paclitaxel-loaded di-block mPEG-PCL copolymer nanoparticles to be implanted into novel targeting hydrogels for pancreatic cancer treatment

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Pancreatic cancer is characterized by dense solid tumors which inhibit the formation and function of blood vasculature, thereby diminishing drug delivery. Active targeting is therefore required in order to achieve effective and selective delivery of the anticancer agent within this complex microenvironment. Polymeric nanoparticles have already offered some unique advantages in cancer treatment. To further enhance their therapeutic index, especially for local administration, nanoparticles have been increasingly combined with hydrogels to form a robust hybrid biomaterial system (NP-gel). In the present study, the biodegradable and biocompatible di-block methoxypoly(ethylene glycol)-poly(caprolactone) copolymers (mPEG-b-PCL) were synthesized and investigated as carriers for the preparation of paclitaxel (PTX)-loaded nanoparticles, which will be further incorporated into a smart, multifunctional polypeptide-based hydrogel system.

The mPEG-b-PCL copolymer was synthesized via ring-opening polymerization (ROP) of ϵ -CL [1], using mPEG as the macro-initiator and stannous octoate [$\text{Sn}(\text{Oct})_2$], as catalyst (initiator/catalyst molar ratio 1:1) (Figure 1). Briefly, mPEG (of several molecular weights) and ϵ -CL were mixed in different molar ratios (1:2, 1:4, 1:5) in a flask connected to a vacuum pump and kept at 150 °C for 1 h under N_2 atmosphere and constant stirring. Then the catalyst was added and the polymerization proceeded at 160 °C for 6 h under increased stirring and a high vacuum [2].

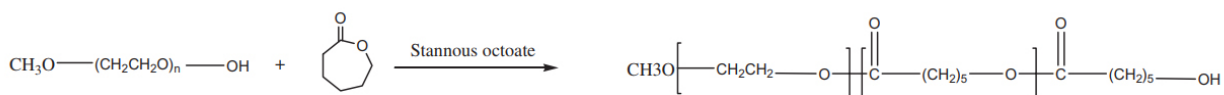


Figure 1. Schematic representation of the synthesis reaction of mPEG-PCL copolymer.

The prepared copolymers were afterwards used to fabricate the PTX-loaded nanoparticles by a single oil-in-water emulsion solvent evaporation technique. In short, 100 mg of the copolymer and 10 mg of PTX were dissolved in 5 mL of DCM and the resulted solution was added in a PVA aqueous solution. The o/w emulsion was stirred until solvent evaporation and the NPs were collected via centrifugation, washed twice, frozen and freeze-dried.

The structure and composition of the synthesized block copolymers was determined by ^1H -NMR and FTIR spectroscopy. DSC, XRD and solubility studies were also performed. The prepared NPs were studied for their size, morphology and drug loading capacity.

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Preparation of salmeterol xinafoate chitosan nanoparticles for chronic obstructive pulmonary disease treatment

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Chronic obstructive pulmonary disease (COPD) is a process characterized by the presence of chronic bronchitis or emphysema that may lead to the development of airways obstruction [1]. Salmeterol xinafoate is an effective long-acting bronchodilator which is used extensively for ameliorating COPD's symptoms [2]. Nevertheless, it is a sparingly soluble drug in aqueous solutions resulting in its poor bioavailability. Chitosan is a natural polysaccharide which has been extensively studied in the past due to its unique properties such as biocompatibility, biodegradability and non-toxicity. Chitosan nanoparticles are prepared by the interaction of oppositely charged macromolecules [3]. The drug molecules may be entrapped onto the nanoparticles, which will help to the amorphization of the drug and to facilitate the penetration through the physiological barrier [4]. In this study chitosan nanoparticles were synthesized via ionic gelation technique with sodium tripolyphosphate as polyanion. Salmeterol xinafoate was enclosed in the nanoparticles. Interactions between the drug and the polymeric matrix were evaluated by FTIR while the amorphous entrapment was confirmed by X-ray diffraction and DSC analysis. DLS and SEM measurements revealed the size and the morphology of the nanoparticles, whereas TGA measurement revealed nanoparticle's thermal stability. In vitro drug release studies were conducted as well. Our results revealed the formulation of nanoparticles and the successful inclusion of salmeterol xinafoate in their interior.

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Nanoencapsulation of pomegranate juice in modified chitosan with enhanced stability and antibacterial properties appropriate for cosmetics

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Chitin, the second most abundant natural polysaccharide, originates mostly from crustaceans. Chitosan, the product of chitin's deacetylation, has been extensively studied due to its unique properties such as biodegradability, biocompatibility and non-toxicity [1]. However, its poor solubility in alkaline pH as well as in organic solvents restricts the applicability of the polymer. An effective way to overcome this restriction is through the modification of chitosan's functional groups. Through this manner new derivatives are produced, characterized by new or improved properties [2]. Pomegranate juice is an important source of bioactive compounds and shows great antioxidant activity attributed to its high content of polyphenols [3].

In the present study chitosan modification was conducted with [2-(methacryloyloxy)ethyl]dimethyl-(3-sulfopropyl)ammonium (SBMA) through a free radical polymerization technique. FTIR spectra confirmed the successful modification and TGA analysis revealed an ameliorated thermal behavior of the polymer. Swelling test was conducted as well in order to evaluate modified chitosan's improved swelling ability. Subsequently modified chitosan nanoparticles were synthesized via ionic gelation technique with sodium tripolyphosphate as polyanion and pomegranate juice was enclosed in the nanoparticles. Interactions between the pomegranate juice and the polymeric matrix were evaluated by FTIR. Size distribution of the nanoparticles was calculated by DLS while SEM images confirmed their spherical size. Our results clearly indicate the successful preparation of modified chitosan, the formulation of nanoparticles and the successful inclusion of pomegranate juice in the interior of the nanoparticles. The prepared pomegranate nanoparticles are intended to be used for the preparation of novel cosmetic formulations with natural ingredients showing enhanced stability and offering advanced skin antioxidant protection against free radicals together with good antibacterial properties.

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Synthesis, structure, and properties of novel biobased polyesters, obtained from furan dicarboxylic acid and new fully renewable diols based on vanillic acid

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Solvent-free synthesis of monomers is one among the most promising ways to develop greener polymers that are both environmentally and economically acceptable, but it was described as one of the “grand challenges” facing chemists [1]. As a contribution towards sustainable polymers development which has gained prominence and has attracted great attention in materials science research nowadays, a truly efficient, practical, and more environmentally friendly *solvent-free* synthetic route was successfully applied herein to prepare three new fully biobased diol monomers derived from vanillic acid and aliphatic diols (ethylene glycol, 1,3-propanediol and 1,4-butanediol). Their chemical structures were confirmed in detail by ¹H, ¹³C NMR and FTIR spectroscopies and their thermal properties were investigated by DSC and TGA. The TGA curves showed no significant weight loss ($T_{d, 5\%}$) up to 243, 284 and 312°C respectively for ethylene glycol, 1,4-butanediol and 1,3-propanediol-based monomers. Indeed, high melting points in the 121.8-142.3°C range were revealed for the three obtained diols. These results showed the effectiveness of the innovative synthetic strategy proposed. To prove their suitability in polymerization, the three prepared diols were successfully polymerized using three reactive diacid chlorides (succinyl chloride, adipic chloride and sebacoyl chloride) by melt polycondensation under free catalyst conditions. The chemical structures of the nine prepared polyesters were confirmed in detail by ¹H, ¹³C NMR and FTIR spectroscopies. The latter showed satisfactory intrinsic viscosity values in the 0.23-0.28 dL/g range and a wholly amorphous nature. All materials underwent a single stage thermal degradation and they revealed high thermal stability with onset degradation temperatures $T_{d, 5\%}$ ranging from 314 to 373°C. These polyesters showed wide glass transition temperature (T_g) range oscillating from -2.8 to 50°C. Extended synthesis towards the preparation of other two new fully biobased furanoate polyesters derived from vanillic acid has been successfully carried out by two-stage melt polycondensation, using Tetrabutyl titanate (TBT) as catalyst. This synthesis involves the combination of 2,5-furandicarboxylic acid (FDCA) with the above-described 1,4-butanediol and ethylene glycol-based diols. Resulting materials showed an amorphous behaviour and excellent thermal stability, exceeding 342.6°C and 366.3°C and T_g values of 13.6 and 69.5°C respectively for the polyesters derived from 1,4-butanediol and ethylene glycol-based monomers. Taking advantage of its excellent and similar thermal properties with those of polyethylene furanoate (PEF) [2], polyester prepared from FDCA and ethylene glycol-based diol has the potential to serve as innovative and promising biobased polyester for practical applications such as sustainable and eco-friendly plastic packaging.

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Preparation and characterisation of modified chitosan with succinic anhydride and trans aconitic acid

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Poor water-solubility of drugs which results in their poor bioavailability, is one of the major challenges in pharmaceutical research. Chitosan, the second most abundant natural polysaccharide, has been widely studied due to its unique properties (biocompatibility, biodegradability and non-toxicity). However, despite its beneficial properties chitosan is an insoluble polymer in organic solvents and in alkaline pH. Chemical modification of chitosan's structure is an effective way to ameliorate its chemical properties and prepare new materials with potential use in different applications [1]. To this end, it has been revealed that the introduction of carboxylic groups is able to ameliorate chitosan's solubility and hydrophilicity [2]. Due to the presence of -NH₂ and -COOH groups in the new structure, modified chitosan is able to react with many kinds of agents and prepare water insoluble drug conjugates [3]. In this study chitosan modification was conducted with succinic anhydride with a ring opening reaction as well as with trans aconitic acid with EDC as an activator of carboxyl groups, respectively. Characterization of the new materials was conducted by FTIR and NMR which revealed the successful grafting of both succinic acid and trans aconitic acid, respectively, into CS macromolecules. The crystallinity of the new materials which was studied using X-ray spectroscopy, revealed the amorphous state of the grafted materials. In addition, TGA analysis was performed to assess their good thermal stability and swelling tests were also conducted in order to evaluate modified chitosan's improved swelling ability. Our results support that chitosan was successfully modified with these monomers.

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Synthesis and characterization of novel cross-linked polyester resins (UPRs) based on succinic acid

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Unsaturated polyester resins (UPRs) are a polymer class asserting a position among the greatest achievements of polymer industry. Their simple processing and the variety of fields of application are the reasons they are considered a breakthrough since the 1930s, when they were firstly produced industrially, and they remained relevant to this day among other cross-linkable materials. In general, UPRs consist of a polymeric matrix with unsaturated double bonds and via radical polymerization they are combined with unsaturated monomers to create a cross-linked network [1,2].

In recent years, due to the inability for proper waste management and the uncertainty surrounding crude oil in terms of price and availability, emphasis is given in the production of polymers from renewable monomers, the so-called bio-based polymers. So, a demand for bio-based UPRs was also created. A bio-based UPR should meet criteria for low cost, hazardless raw materials, no biodegradability and a performance equal or superior to the materials currently in use, in order to maintain sustainability in the chemical industry [3,4].

In this work, UPRs partially based on biobased monomers were prepared. Succinic acid, ethylene glycol and maleic anhydride were used to prepare unsaturated polyester chains. Acrylic acid was used as the reactive diluent, and the cross-linking was made through thermal curing. The physicochemical properties of the prepared materials were examined with ¹H NMR, FTIR, DSC and TGA. From ¹H NMR and FTIR the successful synthesis of the materials was confirmed. With DSC measurements, parameters of the cross-linking reaction were examined and TGA was used to investigate the thermal stability of the cross-linked materials.

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Synthesis and characterization of eco-friendly UPR resins, based on succinic acid, itaconic acid and ethylene glycol

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Unsaturated polyester resins (UPRs) are linear polycondensation products based on unsaturated and saturated acids/anhydrides and diols or oxides. The unsaturation in the backbone provides sites for reaction with vinyl monomers using free-radical initiators, thereby leading to the formation of a three-dimensional network. Unsaturated polyester resins (UPRs) have been known for many years. The production of UPRs started in the 1930s. Polyester resins, because of their versatility and low cost, are widely used throughout the world. UPRs are, along with polyurethanes, the most important cross-linkable polymeric materials. In recent years, due to the increased environmental pollution levels, research focuses on the production of polymers from renewable monomers, the so-called biobased polymers. Succinic acid is a dicarboxylic acid which is a new biobased monomer with a huge market and environmental potential.

This work was based on the production of UPRs from succinic acid. Succinic acid, ethylene glycol and itaconic acid were used to prepare unsaturated polyester resins. The physicochemical properties of the prepared resins were examined with ¹H NMR, FTIR, DSC and TGA.

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1,3-Dioxolane-4-ones: a path to explore toward highly functionalized polyesters

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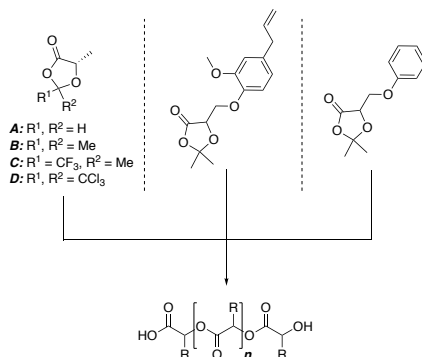
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Within the pursue of environmentally friendly alternatives to oil-derived plastics, polylactic acid (PLA) has emerged as one of the best candidates, thanks to a winning combination of green nature and good processability properties. In addition, PLA is biocompatible and its degradation byproducts are harmless in vivo. On the other side of the coin, however, drawbacks such as poor toughness and poor thermal stability strongly limit its industrial applicability. For this reason, PLA-related research is usually aimed at improving its lacking properties, while preserving its good features. Alongside nanocomposite preparation and blending strategies, the synthesis of highly functionalized PLA-based materials, endowed with tailored properties, is scarcely investigated, due to a reduced monomer scope. Within this field, the development of O-Carboxyanhydrides (OCAs) chemistry appeared as a powerful tool, giving access to variegated structural motifs and easy polymerizations [1]. However, synthesis of OCAs relies on highly toxic reagents and their inherent instability prevents storage for prolonged time. Looking for a new monomer, able to preserve access to structural modification and reactivity while overcoming inefficient synthesis of OCAs, 1,3-dioxolan-4-ones (DOXs) appear as promising candidates. DOXs synthesis is straightforward and their high reactivity is ensured by the release of a small molecule during the polymerization, providing a strong driving force for the reaction. Given the scarce number of reported DOXs polymerizations [2] and aiming to develop a metal-free protocol, we first investigated the reactivity of the lactic acid-derived DOX monomer under protic acids catalysis conditions. The influence of different ketones and aldehydes as protecting groups on the reaction outcome was evaluated. With the aim of expanding potential DOXs applications, a new eugenol-containing DOX monomer was successfully synthesized and polymerized. Thanks to the reaction of both the hydroxy acid moiety and the eugenol allyl chain, a thermoset product was obtained, displaying self-healing and shape memory behavior, as well as remarkable tensile strength properties and complete degradability under basic conditions [3]. Finally, copolymerization studies between a DOX monomer and commercially available L-lactide have been carried out, aimed to achieve an efficient incorporation of phenol-containing, DOX-derived units into a high molecular weight polyester chain.



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Citronellol-based building blocks for the synthesis of fully renewable copolyesters of poly(butylene succinate) containing functionalizable carbon-carbon double bonds

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The application of renewable monomers for the synthesis of polymeric materials has gained significant attention over the last decades from both academia and industry. Driving factors stimulating this research are the depletion of commonly used fossil oil feedstock, the world-wide increase in pollution and greenhouse gas emissions, mainly resulting from the use of fossil oil-based fuels and materials. The application of renewable and degradable materials in daily life represents a valid solution to these urgent and serious problems, contributing to decrease both the pollution and the emission of greenhouse gases, thereby helping to get a cleaner and healthy environment [1,2]. Among bioplastics, poly(butylene succinate) represents a very interesting candidate, being both biobased and biodegradable. Moreover, it shows quite high melting temperature, good mechanical property and recently got the FDA approval.

Although terpenes and terpenoids are considered interesting organic feedstock for the generation of green plastics and composites, due to their natural abundance and low-cost, new approaches are required to transform them into monomers that can produce more competitive polymers. Here we propose the photooxygenation reaction as new and sustainable functionalization of terpenes and terpenoids to transform them into poly-oxygenated compounds to be employed for the preparation of new bio-based polyesters. In this context, citronellol is converted into diol **1** using singlet oxygen ($^1\text{O}_2$), a traceless reagent that can be generated from air, visible light and zeolite supported-photosensitizer (Thionine-NaY). With our synthetic approach, monomer **1** has been obtained in one-step, with good regioselectivity, using green reagents such as light and air, and finally without solvent. Moreover, the supported catalyst can be recover by filtration and reused without loss of activity. In this framework, a citronellol-based copolyester of poly(butylene succinate) has been synthesized and studied. Molecular characterization shows good control of the synthesis conditions preserving the presence of the functionalizable double bonds in the final material. Thermal analysis evidences a reduction of melting temperature and crystallinity degree with respect to PBS homopolymer. Mechanical tests reveal a decrease in elastic modulus of one order of magnitude. The results obtained evidence the copolymerization of PBS with the citronellol-based building blocks proposed allows the obtaining of a more flexible and functionalizable material by exploiting a largely available natural molecule modified through a completely green synthetic path.

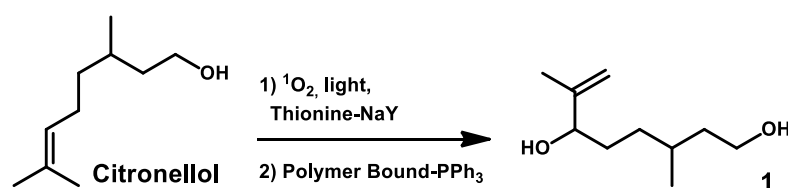


Figure 1. Photooxygenation synthesis of diol **1**.

On a novel method to improve the hydrolysis resistance of polylactide film by POSS surface grafting

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Polylactide (PLA), a bio-based and biodegradable aliphatic polyester, represents one of the most promising, sustainable, alternatives to plastics from fossil sources [1]. Nevertheless, one of the major drawbacks, which limits its use in durable applications, is related to its low hydrolytic stability, compared with other similar polymers [2]. The polymer degradation rate is determined mainly by the polymer reactivity with water and accessibility of the ester groups to water and catalysts, namely carboxylic acid end groups and it is accelerated by the temperature [1]. With the aim at improving such characteristic, several strategies were attempted, which were based on the manipulation of the polymer chemical architecture [3] and on the blending with other polymer systems [4] or with proper fillers/nanofillers [5]. Although the above strategies turned out to modify the polymer degradation, several issues have to be considered for their application, that is: i) the modification of the polymer features such as the transparency and ii) the compatibility of the additives, both organic and inorganic, with PLA and consequently their dispersibility. On this basis, the development of simple methods, not based on severe conditions or complicate instruments, but capable of increasing the hydrolysis resistance of PLA without changing the polymer intrinsic features, represents a key aspect for expanding the polymer applications. Clearly, an ideal approach should be based on the modification of the polymer surface without affecting its bulk.

On this basis, the present work deals with the assessment of an easy and scalable method to modify the characteristics of poly(L-lactide) (PLLA) films, which approach was based on the exploitation of a surface treatment with an amino functionalized polyhedral oligomeric silsesquioxanes (POSS-NH₂). The main idea of the applied technique lays in the potential reactivity of POSS amino group towards the polymer functionalities to give an aminolysis reaction, which should lead to the direct grafting of silsesquioxane molecules on the polymer surface. Both neat and treated films were characterized by FT-IR and XPS measurements, which allowed to prove the effectiveness of POSS grafting. Moreover, FE-SEM characterization demonstrated the homogeneous distribution of Si on the film surface treated with POSS. The effect of the film treatment on the surface wettability was studied by contact angle measurements. These results demonstrated a relevant enhancement of the surface hydrophobicity, which increment turned out to be a function of the conditions applied, as it was found to increase by increasing the reaction temperature and the contact time. Finally, the evaluation of the stability of neat and treated PLLA films was performed by examining the weight loss and the surface morphology after being treated with pH 7.4 buffers at 50 °C for different days. The results evidenced a much higher stability of the treated with respect to the neat PLLA films, which, conversely to the POSS based systems, showed a relevant loss of integrity already after 20 days.

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Polyhydroxyalkanoates/nanocellulose composites for fused deposition modelling

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In recent years the use of sustainable materials has attracted a great deal of attention. Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) (PHBH) is a random copolymer of 3-hydroxybutyrate and 3-hydroxyhexanoate. Possible applications include tissue engineering, production of medical devices and flexible packaging [1]. Nanocrystalline cellulose (CNC) is one of the most interesting reinforcing fillers used in the production of green nanocomposites due to its properties and to the ability to undergo chemical modification [2]. Among the various techniques involved in the processing of bioplastics, relatively little attention has been so far devoted to additive manufacturing (AM) technologies. Fused deposition modelling (FDM), combines the low operation costs with the easy use and the possibility of realizing small and complex objects [3]. In this work, novel PHBH/nanocellulose biodegradable composites for additive manufacturing were produced and characterized. Composites filaments for additive manufacturing were obtained and characterized and the possibility of 3D printing the resulting filaments was investigated.

Polymer granules of PHBH X151A grade, provided by Kaneka Corporation (Osaka, Japan) were used as polymer matrix. Microcrystalline cellulose powder, having a mean particle size of 20 µm and a bulk density of 0.6 g/ml, was purchased from Sigma-Aldrich srl (Milano, Italy). Neat PHBH and nanocomposites filaments were produced by solution mixing and melt-extrusion. The filaments were used to feed a FDM machine. The cryofractured surfaces of both filaments and 3D printed samples were observed through a Zeiss Supra 40 field emission scanning electron microscope (FESEM), operating at an acceleration voltage of 2.5 kV. Relative viscosity measurements were carried out through a Ubbelohde viscometer inserted in a thermostatically controlled water bath at a constant temperature of 30 °C. Thermogravimetric analysis (TGA) was performed through a TGAQ500 thermobalance under a nitrogen flow of 10 ml/min in a temperature interval between 30 °C and 700 °C, at a heating rate of 10 °C/min. The tensile properties of filaments and 3D printed samples were measured at 23 °C through an Instron 4502 tensile machine, at a testing speed of 1 mm/min. Viscosity measurements performed on neat 3D printed samples revealed that no decrease of molecular weight due to the printing process occurred. At higher filler content, the formation of aggregates has been observed through FESEM analysis. From a qualitative point of view, it was observed that the 3D-printing process promoted an increase of the nanocellulose (NC) aggregation tendency. From thermogravimetric analysis it was clear that the degradation behaviour of the 3D printed materials was not substantially affected by NC addition. As far as the mechanical properties is concerned, the nanofiller addition resulted in a reduction of the stiffness of the samples. The reinforcing effect obtained by the presence of nanocellulose was limited to a concentration of 0.5 %. Probably, at higher filler loadings, nanofiller aggregation and interfacial debonding limited the reinforcing capability of the samples. However, the ductility of the materials was not impaired by NC aggregation.

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Thermally reversible thermosets from vegetable oils

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Thermally reversible thermosetting polymers offer a distinct advantage with respect to “classical” thermosets, which is the possibilities for rework and recycling [1]. The use of renewable precursors makes the products even more attractive from an environmental point of view. Vegetable oils are one of the most important renewable resources for the chemical industry [2]. A strategy to use these oils for the synthesis of thermoreversible thermosetting polymers is to attach furan units to their structure and to crosslink the products with maleimide-bearing molecules via the Diels-Alder reaction [3]. The resulting furan-maleimide adducts are thermoreversible due to the retro-Diels-Alder reaction, thus enabling the polymer to be reworked. Oils from *Jatropha curcas* and sunflower seeds were epoxidized, and further reacted with furfurylamine to attach furan units. The temperature, reaction time, furfurylamine concentration, and catalyst loading were optimized to maximize the number of furans attached to the epoxide sites instead of the esters. This is important in obtaining enough functionalities to form a network structure. The furan-derived oils were reacted with two types of bismaleimides in different compositions. It was found that the rigidity of the polymers was influenced by the structure of the modified oil and the composition of the bismaleimides.

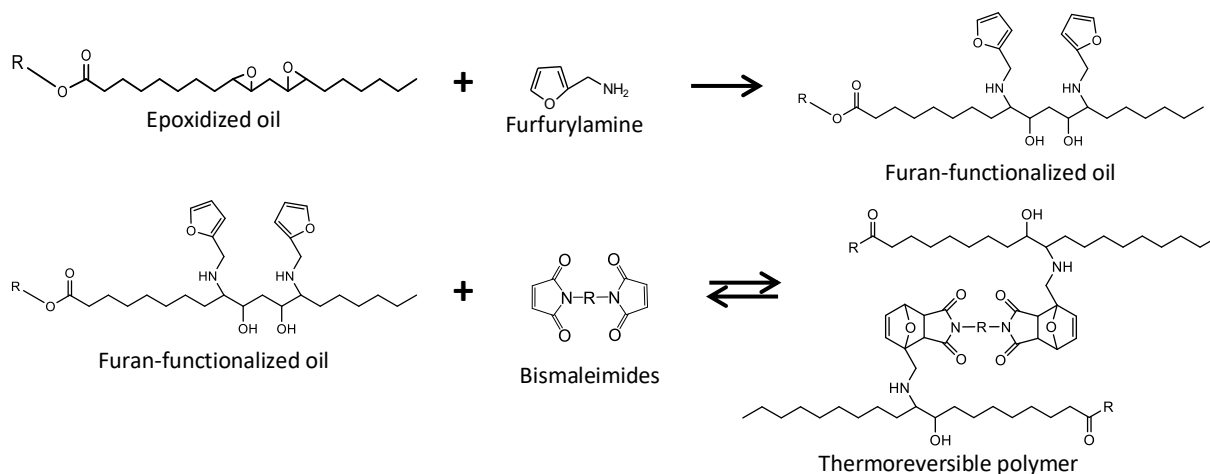


Figure 1. The proposed route towards thermoreversible polymers from vegetable oils.

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Ministry of Research, Technology, and Higher Education of Indonesia.

Multi-approach strategy for the development of highly performant polymer composites based on phthalonitrile resin, tungsten carbide nanoparticles, and carbon fibers

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Phthalonitrile resins as one of the leading high performance polymers are currently used in highly exigent applications. Herein, aiming to achieve the best combination of mechanical, thermal, and nuclear shielding performances, we prepared hybrid materials based on the typical phthalonitrile resin and the silane surface modified chopped carbon fibers and tungsten carbide nanoparticles. The obtained results suggested that a synergistic combination between the three constituents was clearly achieved leading to excellent mechanical and gamma rays shielding properties. For instance, the tensile and bending strengths reached up to 505 and 584 MPa for the composite containing 20 and 30 wt.% of carbon fibers and tungsten carbide nanoparticles, respectively. Similarly, the gamma rays screening ratio also reached the exceptional value of 39% for the same 2 cm thick hybrid. Finally, the as such described hybrid materials proved that a multi-approach strategy is often the best solution to achieve the requirements of highly exigent applications.

Acknowledgments

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Halloysite nanotubes as promising candidates for the preparation of polyamide-6 nanocomposites

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Halloysite is a polymorph of kaolinite which naturally wraps itself to form tubular structures. Due to its availability, low cost and morphology, it has gained attention in numerous fields of application, including functional coatings and polymer nanocomposites [1]. It is particularly suited to the filler role as it is cheap, thermally and mechanically resistant, and characterized by a high aspect ratio, crucial to guarantee strong polymer-filler interactions [2]. Clay powders are widely adopted as flame retardant additives at high percentages. The application of halloysite nanotubes (HNT) as additives at low contents for the tailoring of the mechanical and thermal properties of polymer composites has been instead much less investigated [3]. Our group investigated the use of HNT as additive at low content (< 5%w) in polyamide-6 (PA6) nanocomposites, due to its wide range of industrial application and relatively poor thermal and mechanical properties. Two different commercial HNT samples were adopted, showing different aspect ratios and purity (Fig. 1). The surface properties of both materials were modulated by functionalization with (3-aminopropyl)triethoxysilane (APTES). Samples were extensively characterized by TEM, BET, FTIR spectroscopy and ζ -potential measurements. Both extrusion and one-pot synthesis preparation were tested, and the resulting nanocomposites were characterized by TGA, DSC, DMA and rheology measurements. Preliminary results suggest that the addition of HNT produces an increase in the crystallization temperature; the presence of HNT in the polymer matrix appears to favour the formation of the γ -phase of PA6. While APTES functionalization eased the filler incorporation during extrusion, it lowered the viscosity of the starting polymer. The obtained results suggested a large room for tunability of the properties of PA6/HNT nanocomposites.

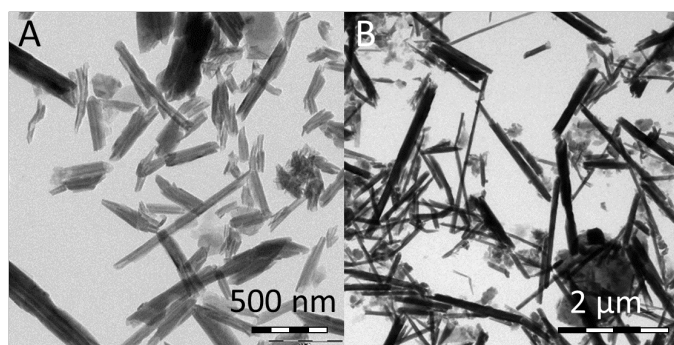


Figure 1. TEM images of the two HNT batches: those from Sigma-Aldrich (A) and those from iMinerals (B).

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PANI-TiO₂ composites: the mechanism behind a green process

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Polyaniline (PANI) is an important member of the family of organic conductive polymers, which holds potential in numerous fields, such as electronics, optics and photovoltaics [1]. In recent years, PANI has received increasing attention for application in wastewater treatment due to its sorption properties enabling the removal of a broad range of pollutants [2,3]. Polyaniline is classically synthesized by oxidative polymerization [4], which involves noxious reagents (aniline as starting compound and persulfates as oxidant) and gives rise to toxic and carcinogenic by-products (such as benzidine and *trans*-azobenzene). A great deal of effort has been devoted to find alternative green routes: in particular, some of us reported a benign synthesis based on aniline dimer ((4-aminophenyl)aniline), H₂O₂ as oxidant and Fe³⁺ as catalyst [5]. However, this procedure yields no control on the polymer morphology, leading to a compact PANI with low surface area and poor dye sorption capability. We have recently developed an alternative green synthesis based on TiO₂ photocatalysis, enabling a morphological control of the polymer [6]. In this work, the reaction mechanism has been investigated in depth via LC-MS, FT-IR and ζ -potential analyses. In the first stage, carried out under UV irradiation, the growth of oligomers from the aniline dimer takes place on the TiO₂ particle surfaces, activated by the photocatalytic generated radicals. In the second step, the addition of H₂O₂ (80% less than in the Fe-catalyzed synthesis) activates the polymer growth, giving rise to the final product. By separating the oligomerization and polymerization steps, polymer composites with high crystallinity and porous morphology could be prepared. The dye sorption capability of the samples was tested toward methyl orange as model for anionic azo dyes: promising results were obtained both in terms of dye removal and product reusability. The creation of PANI-TiO₂ composites opens the door to future applications exploiting the complementary properties of the two materials, such as pollutant removal processes based on combined sorption and photocatalytic degradation.

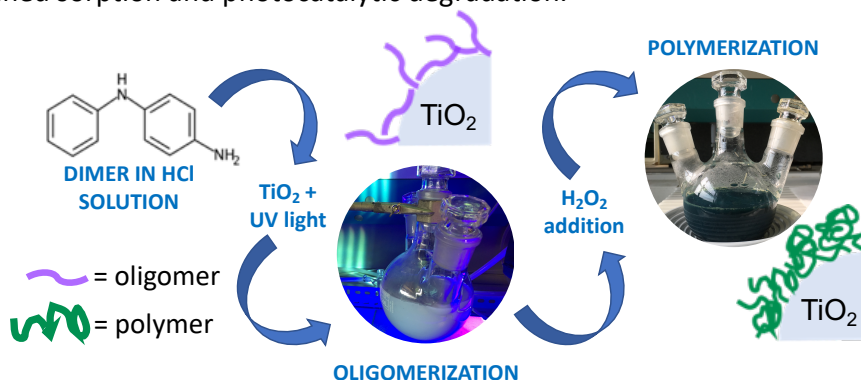


Figure 1. Outline of the reaction mechanism.

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Polymer protected metal nanoparticles as catalyst for liquid phase reactions

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Studies on gold catalysts for the synthesis of fine chemicals in liquid phase have recently received a lot of attention [1]. In particular, the preparation route, involving the immobilisation of preformed gold nanoparticles, has become very popular as this method allows a fine-tuning of the particle size and shape [2]. However, the role of the protective agent is still not completely understood even the positive effect on the durability of catalyst was reported [3]. The present study reports on the synthesis and catalytic testing of gold nanoparticles protected by different polymers, i.e. polyvinyl alcohol (PVA) (Fig.1) and polyvinyl pyrrolidone (PVP). Different amounts of protective agent were used to highlight the role of the thickness of the protective layer on the catalytic activity and the selectivity in the liquid phase oxidation of glycerol. We found that PVA protected Au nanoparticles (Au_{PVA}) are more active than PVP protected ones (Au_{PVP}). The pyrrolic groups of PVP bind directly to the metal, rendering active sites not accessible to the reactant [4]. By decreasing the amount of PVA, the catalyst becomes more active, but the selectivity to glycerate decreases. This behaviour in the selectivity is probably due to a different adsorption mode of glycerol on the Au active sites in presence of a different PVA amount. Characterizing the catalysts by means of XRD and HRTEM analyses, we found that by decreasing the amount of PVA, larger Au particles were obtained although a high metal dispersion was maintained.

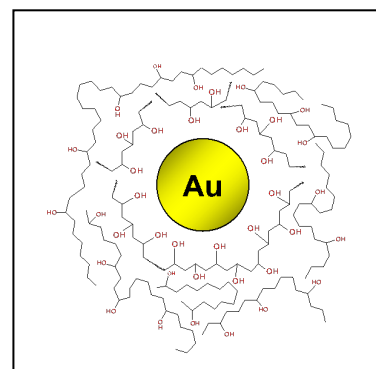


Figure 1 Representation of Au_{PVA} nanoparticles

We conclude that the thickness of the protective layer plays an important role in determining the activity and the selectivity of the reaction. Recycling tests were also performed to analyse the influence of the amount of protective agent on the stability of the catalyst.

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Surface modified polymers as emerging materials for photocatalytic and photoelectrochemical water splitting and air purification

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Photocatalytic and photoelectrochemical water splitting is a very promising approach of the converting solar light into storable chemical energy (fuels). This technology provides an alternative route to the current unsustainable use of fossil fuels, addressing the increasing demand for energy and fuels as well as environmental issues such as high level of CO₂ in atmosphere.

As an alternative to classic photocatalysts, such as metals oxides (e.g. TiO₂, Cu₂O, ZnO, Fe₂O₃), semiconducting polymers have appeared as an interesting class of photocatalysts not only for water splitting but also for CO₂ reduction and organic pollutants removal. The biggest advantage of polymer photomaterials is the possibility of the modification of their electronic and structural properties at a molecular level [1].

Recently, we have studied the use of copper oxide-based materials for photoelectrochemical water reduction to hydrogen [2-3]. These photocatalysts showed high activity and good stability due to self-protecting effect. Subsequently, CuO particles has been deposited onto graphitic carbon nitride (g-C₃N₄) matrix resulting in promising material for hydrogen evolution. Prepared materials showed improved photoelectrochemical activity in comparison with neat g-C₃N₄ and higher photocatalytic activity in comparison with neat copper oxide [4]. Visible-light irradiated composite generates cathodic photocurrents under middle bias with density even several times higher than g-C₃N₄. The band bending existing in type II heterostructures (CuO/ g-C₃N₄) drives the photogenerated electrons and holes to move in opposite directions, resulting in a spatial separation of the photogenerated charge carriers on different sides of heterojunction. Lower recombination rate and higher activity are the overall effect. Gas chromatography detection proved the formation of hydrogen under visible light irradiation in both, photocatalytic (in suspension) and photoelectrochemical (biased electrode) experiments. Moreover, polymer photocatalyst such as graphitic carbon nitride modified (surface) or doped (volume) by transition metals as well as composite of graphene / graphitic carbon nitride and graphene / metal titanates showed impressive activity towards degradation of organic pollutants (e.g. VOC). Therefore, it can be used in air purification systems.

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Monodisperse fiber-like micelles with controllable length: preparation and their colloidal stability in aqueous solution

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In contrast to other kinds of nano-carrier systems, polymer micelles have extensive potential applications in cancer therapy because of their variety in species and their modifiability in structure. Previous studies on fiber-like micelles used as nano-carriers in drug delivery indicated that they can circulate much longer in blood than spherical drug-loaded micelles [1]. However, the method used to prepare the fiber-like micelles with the length ranging from 2 μm to 18 μm , was complicated and the obtained fiber-like micelles had rather broad length distribution. Due to the special enhanced permeability and retention (EPR) effect in tumor tissues, it is of more significance to study fiber-like micelles with lengths below 2 μm . At the moment, precise control over the fiber length has been realized by Winnik, Manners and co-workers by self-seeding [2] and seeded-growth [3] strategies of crystallization-driven self-assembly (CDSA), which are also applicable to other crystallizable polymers. The PFS-based polymer system has already been intensively investigated; there is urgency to extend the applications of these uniform fibers. Inspired by these results, we combine photoactive, electroactive, crystallizable oligo (*p*-phenylenevinylene) (OPV) with biocompatible, water-soluble, modifiable poly(*N*-(2-hydroxypropyl) methacrylamide) (PHPMA) to make a series of rod-coil diblock copolymers with the same OPV segments, but different PHPMA chain lengths. We prepared via the self-seeding process in alcohol solution monodisperse fiber-like micelles with an OPV core, a uniform width and a narrow length distribution ($L_w/L_n < 1.14$). Significantly, the average length of the fiber-like micelles can be precisely tuned by annealing temperature, which resembles the results that Winnik *et al* reported on PFS system [2,3] and in our previous work [4]. Via the self-seeding process (Figure 1), we prepared a series of rod-coil diblock copolymers with the same OPV segments, but different PHPMA chain lengths. These copolymers can form fiber-like micelles in ethanol. Comparing with our previous system OPV₅-*b*-PNIPAM, OPV₅-*b*-PHPMA displays much wider length range of the fibers with much narrower temperature range. That is, our system is more sensitive to temperature variation. Besides, the maximal reachable uniform length of the fiber-like micelle is in the scale of micrometer (2 μm), while OPV₅-*b*-PNIPAM system has not exceeded 800 nm [4]. By taking advantage of the crystalline property of OPV segment, we are able to prepare monodisperse fiber-like micelles with precise control over the length ranging from about 100 nm to 1 μm by “self-seeding” of crystallization-driven self-assembly. Furthermore, we found that among the five kinds of OPV₅-*b*-PHPMA, only OPV₅-*b*-PHPMA₃₆ with a moderate length of PHPMA are colloiddally stable after dialyzed into water, which is out of our theoretical expectation.

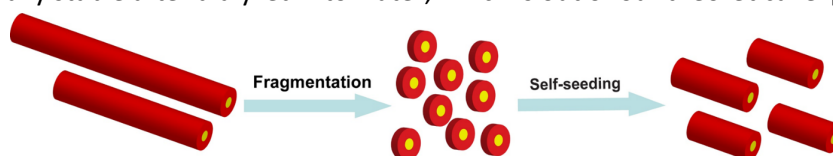


Figure 1. Schematic illustration of self-seeding process.

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A new approach for the electrochemical and structural characterization of newly received tea stains-inspired macromolecules *via* temporally-controlled *se*ATRP

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The headline aim of our research is a synthesis of novel tannic acid-based polymers in two-step synthetic route. At the beginning naturally-derived initiator with twenty bromine initiating sites was synthesized by the transesterification reaction of tannic acid with 2-bromoisobutyl bromide (BriBBR). Subsequent, according to the “grafting from” solution, a series of multi-armed bioinspired star-shaped macromolecules with a hydrophilic tannic acid core and poly(butyl acrylate) (PBA) arms was received *via* a multiple-step potential electrolysis procedure utilizing copper(II) bromide/tris(2-pyridylmethyl)amine ($\text{Cu}^{\text{II}}\text{Br}_2/\text{TPMA}$) catalyst complex.

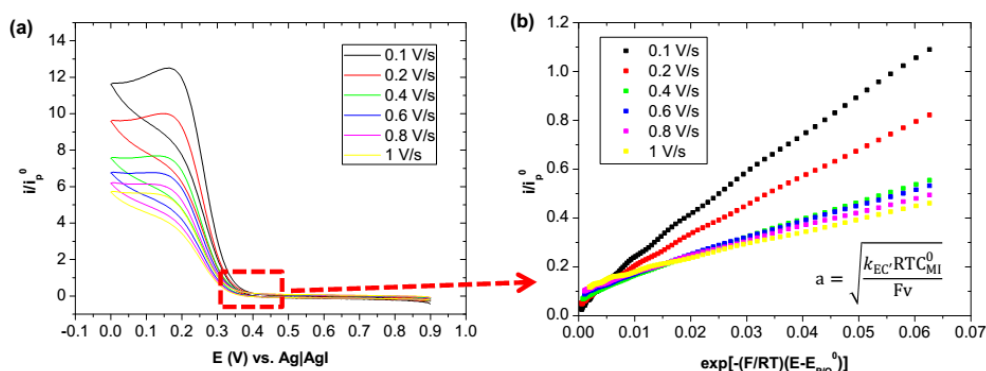


Figure 1. Normalization of the current toward the peak current of a one-electron reversible wave at the same scan rate a) CV responses b) foot-of-the-wave-analyses (FOWA).

Previously cyclic voltammetry was used for the electrochemical characterization of the reaction system in order to kinetic analysis of the electrochemical catalytic process (EC') during reduction of the regenerated $\text{Cu}^{\text{II}}\text{Br}_2/\text{TPMA}$ in the presence of obtained tea stains-inspired macroinitiator. FOWA was used to determine the rate constant of the electrochemical catalytic process ($k_{\text{EC}'} = 6.7 \cdot 10^4 \text{ M/s}$) on the basis of a curve slope (a) of the dependence on the Figure 1b [1]. Preparative electrolysis demonstrated the possibility of temporal control. This approach creates the possibility of stopping and restarting of the polymerization by switching the “off” and “on” stages, respectively, while maintaining the well-controlled characteristic of the process. Average particle diameter determination and confirmation of the architectures of received macromolecules was conducted by atomic force microscopy (AFM) technique (Figure 2). Proposed switchable tannins-inspired product will have tremendous potential in biosensor application, including stimuli-responsive drug delivery systems.

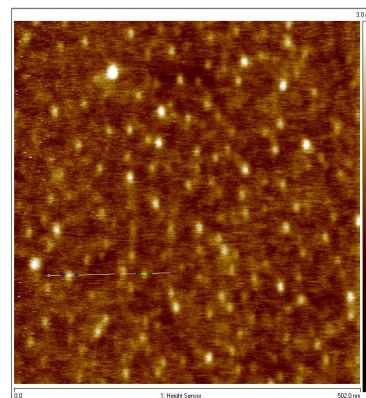


Figure 2. AFM image of tannins-based macromolecules

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Keratin and coconut fibres from mexican industrial wastes as flame retardant agents on thermoplastic starch biocomposites

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Natural fibres have been thoroughly investigated in polymer composites science since many years ago. The main application of natural fibres has been as mechanical reinforcement [1]. However, in the last years the researches have been focused on new applications, such as flame retardant materials [2]. In this work keratin and coconut fibres, recovered from Mexican industries wastes were investigated as multifunctional agents: mechanical reinforcement and flame retardants. A specific treatment was applied to fibres in order to obtain biopolymer composites base on biodegradable thermoplastic starch. The biocomposites were compounded by extrusion process. The effect of keratin and coconut fibre content and the joint action of fibres in combination with ammonium polyphosphate as fire retardant additive, for biodegradable thermoplastic starch was studied by thermogravimetric analyses, UL94-V method, forced flaming combustion, mechanical and rheological analysis. It was found that when keratin or coconut fibres are added in combination with ammonium polyphosphate additive to biodegradable thermoplastic starch a synergistic effect leads to replace part of ammonium polyphosphate using 20% of keratin or coconut fibers. Keratin fibres and ammonium polyphosphate showed the same flame retardant properties. Coconut fibres and ammonium polyphosphate exhibited lower heat release rate than only ammonium polyphosphate at high content (20%). According to rheological measurements, flow behavior depends on the composition of biocomposites, Complex viscosity increases when keratin fibres are added in combination with ammonium polyphosphate with respect to biocomposites using high fibre content. Nevertheless, the combination of coconut fibres with ammonium polyphosphate showed a decrease on complex viscosity favoring the processing of these materials. This finding represents a promising alternative to produce ecological flame retardants and to reduce high waste from the Mexican industry.

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Microfluidics for precise viscosity measurements application: intrinsic viscosity and average molecular weight

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The visual microfluidic rheometer, FLUDICAM^{RHEO}, offers a way to quickly determine average molecular weight by using viscosity measurements. The co-flow microfluidic system uses a small sample volume and can be used for a wide range of viscosities over a very wide range of shear rates (up to 10^5s^{-1}). FLUDICAM^{RHEO} is particularly sensitive for low viscosity solutions which makes it an ideal method for accurate molecular weight determination. The user-friendly design of the instrument and software means that the method is suitable for fast quality control and routine testing without an expert operator.

Visual Microfluidic Rheometer Technique

FLUDICAM^{RHEO} uses a co-flow microfluidic principle to measure viscosity. The sample and a reference solution are simultaneously introduced into the microfluidic channel (typically 2.2 mm X 150 μm) with controlled flow rates. This results in a laminar flow where the interface position between sample and reference relates the viscosity ratio and flow rates. Images acquired during the measurement allow the software to calculate the position of the interface and directly plot an interactive flow curve.

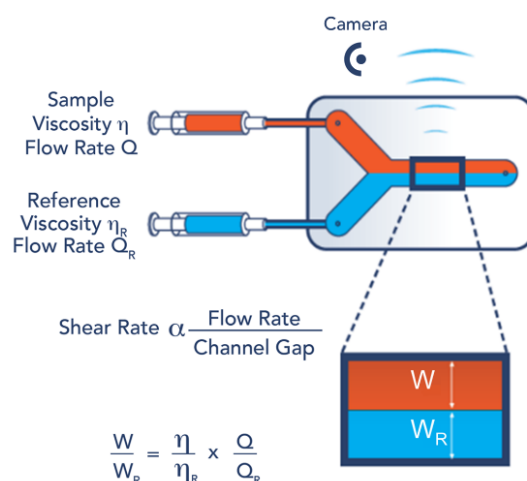


Figure 2: FLUDICAM^{RHEO} measurement principle.

Average Molecular Weight Determination

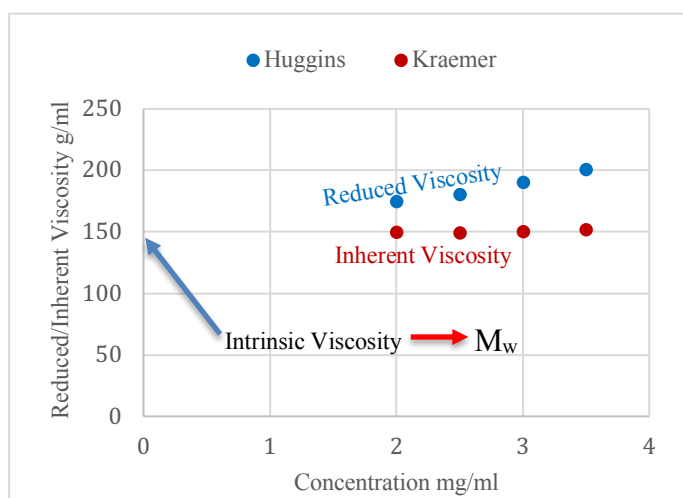


Figure 3: Huggins-Kraemer Plot for hydroxyethyl cellulose solutions.

FLUDICAM^{RHEO} can be used to measure the viscosity of polymer solutions to determine the intrinsic viscosity which is related to molecular weight by the Mark-Houwink equation. The example shown in figure 2 is a hydroxyethyl cellulose polymer. The polymer is fully dissolved in a chosen solvent at a concentration inferior to its C^* . Multiple concentrations can be made up to produce a Huggins-Kraemer plot to determine the intrinsic viscosity graphically, see figure 2. Alternatively, the Solomon-Ciuta equation using a single concentration for an even faster determination.

The PCR proposal for packaging

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The Product Category Rules (PCR) are the basic tools to formulate sound Environmental Products Declarations (EPD) to enable the relevant stakeholders to generate consistent results when assessing products of the same product category. These Rules stem from internationally assessed Norms.

The framework of this document is based on the main functions of packaging as stated in the ISO definition [1]: "Packaging": product to be used for the containment, protection, handling, delivery, storage, transport and presentation of goods, from raw materials to processed goods, from the producer to the user or consumer, including processor, assembler or other intermediary.

Packaging and packaging activities involve all industrial sector stakeholders: packaging manufacturers, users and end consumers. In particular, packaging manufacturers come up with new packaging products and new solutions through intense design and co-design work in collaboration with their customers. It is evident how the packaging sector is marked by extreme complexity and continuous product and process innovation.

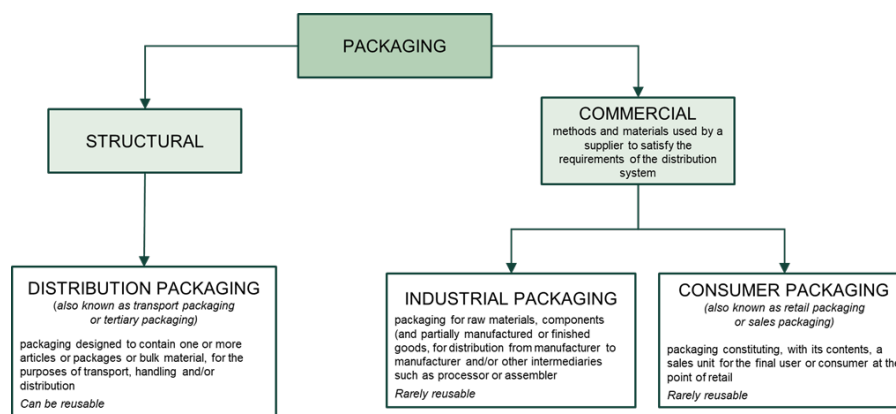


Figure 1. The Packaging structure.

In the packaging sector, it is therefore crucial to establish shared rules that are capable of addressing the diverse needs of users and, concurrently, to recognize the innovative proposals coming from the packaging manufacturers and provide reliable Life Cycle Assessment studies (LCA).

The novelty of this comprehensive approach is presented and discussed.

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1. ISO 21067-1, Packaging – Vocabulary- Part 1: general terms.

Self-structuring in water of polyamidoamino acids with hydrophobic side chains deriving from natural α -amino acids

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Polyamidoamino acids (PAACs) are a novel class of chiral polymeric materials that were recently synthesized and characterized both experimentally and through atomistic computer simulations [1,2]. PAACs can be obtained by polyaddition of *N,N'*-methylenebisacrylamide with natural aminoacids: the first example was obtained with *L*-arginine [1,2], which showed a very interesting and peculiar self-structuring in water, probed by circular dichroism and modeled by molecular dynamics simulations. Here we report the synthesis, the acid-base properties and the self-structuring in water of chiral PAACs obtained with non-polar *L*-alanine, *L*-valine and *L*-leucine (M-*L*-Ala, M-*L*-Val, M-*L*-Leu) with potential for selective interactions with biomolecules [3]. The polymers maintained the acid-base properties of amino acids and in water, while the circular dichroism spectra revealed a pH-dependent structuring. The atomistic molecular dynamics simulations showed that also in these polymers the PAACs assume stable folded and quite compact conformations. The intramolecular interactions lead to transoid arrangements of the main chain reminiscent of protein hairpin motif. Furthermore, oligomers with ten repeat units had simulated gyration radii consistent with the hydrodynamic radii obtained by dynamic light scattering [3].

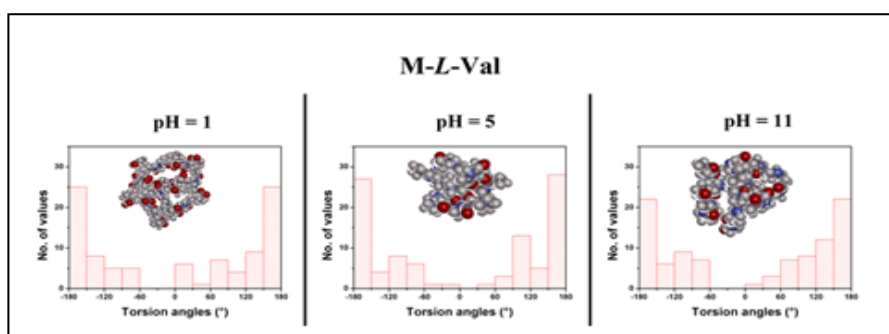


Figure 1. The main chain conformation and the distribution of torsion angles along it for the PAAC with *L*-valine as an example of the general behavior.

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Cyclodextrin nanosponges as *o*-toluidine sorbents

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Hydrophilic cyclodextrin (CD) nanosponges in which the glucopyranoside macrocycles were covalently linked by connecting arms deriving from 1,4-bisacryloylpiperazine or 2,2-bisacrylamidoacetic acid (BAC) were synthesized from α -, β - and γ -cyclodextrins by eco-friendly procedures and tested as sorbents of *o*-toluidine, a carcinogenic wastewater contaminant [1]. The sorption ability of CD nanosponges and that of parent α -, β -, and γ -CDs was determined by monitoring the depletion of *o*-toluidine from 10^{-4} M (10 ppm) aqueous solutions in batch reactors under mild magnetic stirring. The absorption kinetics were registered by monitoring the decrease of the *o*-toluidine voltammetric peak currents in linear sweep voltammetry experiments using multi-walled carbon nanotubes-modified glassy carbon electrodes [2,3]. The experimental curves fitted a mono-exponential kinetic model, indicating a good homogeneity of the sorbent materials. In all cases, the analytical technique revealed *o*-toluidine abatement down to 0.16 ppm, lower by one order of magnitude than the figures from all other sorbents so far reported [4]. Under the adopted conditions, that corresponded to those usually found on the field in *o*-toluidine polluted aquifers, the absorption capacities ranged from 88 to 199 $\mu\text{mol g}^{-1}$ (10-21.3 mg g^{-1}), mostly depending on the type and content of the cyclodextrin moieties and, to a minor extent, to the type of connecting arms. The observed capacities in terms of $\mu\text{mol o-toluidine}/\mu\text{mol cyclodextrin}$ were very close to those of parent CD in case of BAC- γ -CD, higher of a 1.3-1.6:1 factor for β -CD- and a 3.2:1 factor for α -CD-based nanosponges, indicating the presence, in these nanosponges, of cooperative effects among adjacent CD units in the complexation of *o*-toluidine. All nanosponges were completely regenerated by extracting with methanol. After regeneration, the absorption capacity slightly improved, suggesting a rearrangement of the nanosponge network. Overall, it may be reasonably concluded that the CD nanosponges reported in this paper warrant potential as *o*-toluidine exhaustive sorbents.

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Synergism between graphene oxide nanoparticles and disulphide-containing polyamidoamines for enhancing the flame-retardancy of cotton fabrics

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Bioinspired polyamidoamines containing disulphide-groups in the main chain (SS-PAA), prepared by Michael polyaddition of L-cystine with 2,2-bis(acrylamido)acetic acid (B-CYSS), N,N'-methylenebisacrylamide (M-CYSS) and 1,4-bis(acryloyl)piperazine (BP-CYSS), have been recently investigated as intumescent surface-confined flame retardants for cotton textiles [1,2]. B-CYSS proved endowed with superior flame-retardant properties compared with sulphur-deprived polyamidoamines of similar structure whose efficacy had been previously demonstrated. At 12% add-on, B-CYSS inhibited ignition in both horizontal- and vertical flame spread tests (HFST and VFST) [3]. This result was tentatively attributed to the release of H₂S from the cystine moieties, due to the retro-Michael elimination reaction, which acted as radical scavenger in the gaseous phase quenching the oxidation reaction [3]. Similarly, also M-CYSS and BP-CYSS inhibited cotton combustion in VFST, albeit at higher add-ons: 16 and 20%, respectively. Preliminary combustion tests performed on sulphur-deprived PAAs combined with cellulose derived graphene oxide (nGO) [4] did not reveal significant improvements on their flame retardant effectiveness. Interestingly, however, it was found that nGO, acting as thermal conductors, lowered the temperature at which PAAs started intumescenting.

The objective of this work was to investigate if a synergism as flame-retardants of cotton between the above-mentioned SS-PAA and cellulose-derived nGO existed. To this aim, cotton fabrics previously treated with 1% nGO were coated with SS-PAA at add-ons 8%, 12% and 15% for B-CYSS, M-CYSS and BP-CYSS, respectively. At the same add-ons, the corresponding amount of SS-PAA alone neither extinguished nor inhibited cotton combustion in VFST, and nGO had no effect alone. In VFST tests, the B-CYSS, M-CYSS and BP-CYSS extinguished the flame, with little afterglow. VFST tests performed in parallel with cotton fabrics treated with SS-PAA and nGO at the same add-ons confirmed the previously mentioned negative results (Figure 1). These tests demonstrated that a synergism definitely existed between nGO and SS-PAA.

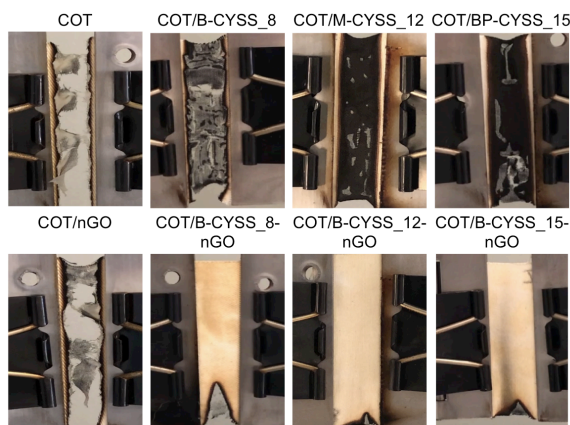


Figure 1. Snapshots of vertical flame spread tests for cotton treated with SS-PAA-nGO and SS-PAA.

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Preliminary tests on the degradation of polyamidoamines in soil and in hydrolytic media

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Linear polyamidoamines (PAAs) are a family of polymers obtained from the Michael type polyaddition of bis-acrylamides and primary or bis-secondary amines. They have been extensively studied for biotechnological applications and as heavy metal ion complexing agents [1,2]. Some copolymeric PAAs containing glycine and guanidine units are endowed with antibacterial and antimycotic activity and could be employed in agriculture, but only if any risk of permanent soil contamination is excluded. PAAs were found to degrade in aqueous solution, but no studies on PAA mineralization in soil are presently available. The aim of this work is filling this gap. A typical PAA prepared by polyaddition of glycine with N,N'-methylenebisacrylamide (MBA-Gly) was chosen as model compound. The soil burial degradation tests were performed in a biometric flask by monitoring the CO₂ produced by the mineralization of an MBA-Gly sample in a closed chamber, following a method described in the literature [3]. A three-layer configuration was adopted consisting of an intermediate layer of natural soil containing the dispersed PAA sample and placed between two layers of porous inactive vermiculite (Figure 1). An aqueous KOH solution placed in a beaker inside the chamber absorbed the released CO₂. The amount of absorbed CO₂ was determined by titrating at intervals the excess KOH, replacing the solution in the system after each measurement. The amount of CO₂ released by the system was compared with that released by two reference systems, namely buried filter paper and a blank chamber containing only soil. All tests were carried out at 25°C. The results were expressed as the difference between the CO₂ absorbed in the PAA-containing flask and those absorbed in the blank system. This test will be expanded to a small library of PAAs, synthesized from the combination of three bis-acrylamides with three amines. Hydrolytic degradation tests were carried out in TRIS buffer solution at 20 mg/mL concentration by monitoring the decrease of molecular weight by means of size exclusion chromatography. In soil degradation, the set-up of the method brought to the complete identification of the correct protocol to follow during sample preparation, incubation and titration. Hydrolytic degradation shows, after 7 days, a decrease of molecular weight of all the PAAs taken into account.

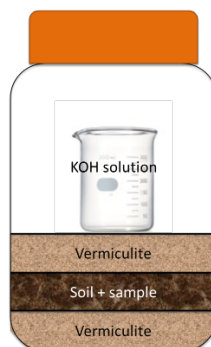


Figure 1. Schematic view of the biometric flask used for soil microbial degradation.

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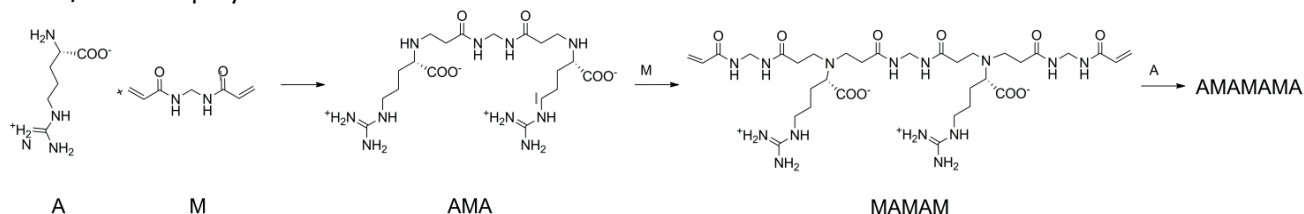
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Controlled synthesis of polyamidoamino acids

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Polyamidoamino acids (PAAC) are bioinspired polymers obtained by Michael polyaddition of natural L- α -amino acids or their D- and D,L- stereoisomers with bisacrylamides at r.t. preferably in water at pH ≥ 9 without organic solvents and added catalysts [1]. They are an off-spring of polyamidoamines (PAAs) obtained from bisacrylamides and amines. In preliminary studies, most PAACs and PAAC/amine copolymers proved biocompatible [2] and, if chiral, capable of assuming stable, pH-dependent conformations in aqueous media [3]. They represent promising candidates for biological applications, for which structure-controlled and narrowly polydisperse polymers would be far preferable. As for molecular weight control, the polyaddition of amines and α -amino acids with bisacrylamides normally gives highly polydisperse ($PD \approx 2$) products. Moreover, in PAACs deriving from amino acid mixtures and in PAAC/amine copolymers, the different units are randomly distributed along the polymer chain. Here we present a strategy for preparing PAAC- and PAAC/amine copolymers with controlled molecular weight (MW) and sequence of the repeating units without the need for either the addition of specific reagents or cumbersome protection/deprotection procedures. This strategy exploits the different reactivity existing between the amine hydrogens of α -amino acids as well as the low solubility of α -amino acids and their oligomers in organic solvents [1]. This allowed synthesizing oligomeric building blocks and proceeding further. In a first instance, one mole of bisacrylamide (M) and two moles of α -amino acid (A) gave nearly pure AMA trimer after 4 days at 20-25 °C; in a second instance, one mol of A treated with a large excess of M and forcing the reaction by warming at 65-70 °C for 4 days gave on lyophilization a mixture of MAM trimer and excess M, removed by dissolving in methanol and reprecipitating with acetone. Proceeding further, the AMA trimer treated with a large M excess at 40-45 °C for 4 days gave a mixture of MAMAM pentamer and M, removed as above; MAMAM treated with two moles of A at room temperature for 3 days gave the AMAMAMA heptamer, and so on. The proof of principle of this procedure was achieved with A = L-arginine and M = N,N'-methylenebisacrylamide (Scheme 1). The heptamer had MW 1160 Da. All α,ω -M-terminated products were used for straightforwardly preparing PAAC/PAA copolymers with controlled sequences of amino acids and amines along the polymer chain. In this case, the proof of principle was achieved by performing polyaddition reactions of piperazine (P) with the MAM trimer and the MAMAM pentamer, obtaining copolymers with regular sequences $[PMAM]_n$ and $[PMAMAM]_n$, with MW 6511 Da (PD 1,11) and 4835 Da (PD 1,09), respectively after a single ultrafiltration step through a membrane with MWCO 3000. The strategy here presented allows to obtain PAACs with controlled MW and narrowly polydisperse PAAC- and PAAC/amine copolymers with a fine structure control.



Scheme 1. First steps in molecular weight control synthesis with L-arginine.

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Hydrophobic polyamidoamines: a new class of technological material?

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Polyamidoamines (PAAs) are biocompatible and degradable synthetic polymers obtained by Michael-type stepwise polyaddition of *prim*- or *sec*-amines to bisacrylamides. PAAs have shown interesting applications in drug and protein intracellular carriers, transfection promoters, antiviral, antimalarial agents and, in the form of hydrogels, as scaffolds for tissue engineering [1,2]. PAA hydrogels do not have mechanical properties that allow them to be used as implantable materials. In order to overcome this problem, different PAA composite hydrogels were investigated, involving either inorganic fillers [3] or PLLA mats [4]. An alternative approach was now attempted. Hydrophobic PAAs have been prepared combining semi-crystallinity, sufficient mechanical strength that is largely maintained in aqueous systems. In particular, PAAs were prepared from long-chain aliphatic bisacrylamides and bis-*sec*-amines or N,N-dialkyl substituted diamine. Dodecamethylenbisacrylamide (DDMBA) and hexamethylenbisacrylamide (HEXAMBA) were obtained by Schotten-Baumann reaction involving acryloyl chloride and 1,12-diaminododecane or 1,6-diaminohexane. The amine monomers were piperazine, N,N'-dimethyl-1,6-hexanediamine, N,N'-dimethyl-1,2-ethanediamine, N,N-dimethyl-1,2-ethanediamine, N,N'-dibenzyl-1,2-ethanediamine, N,N'-diethyl-1,2-ethanediamine. Polymers were synthesized in benzyl alcohol solution at 60°C. The resultant PAAs were characterized by FT-IR/ATR and NMR spectroscopy. Their thermal properties were also investigated by DSC and TGA analyses. As a rule, they showed good thermal stability, with decomposition onset $\geq 200^{\circ}\text{C}$, and partial crystallinity. Films were obtained by both solution casting and compression molding. The ignitability of PAAs was assessed applying a methane flame for 10 s directly to the dried polymer powder placed on a ceramic backing pad. All hydrophobic PAAs never ignited.

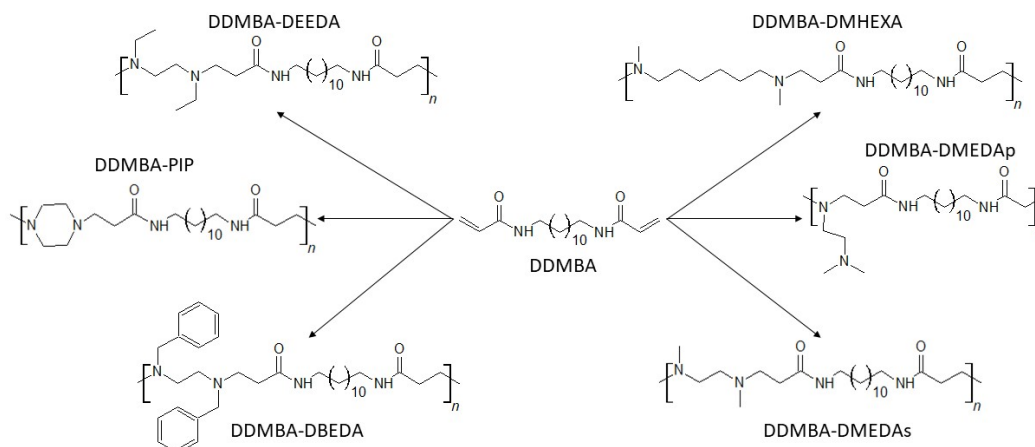


Figure 1. PAAs from dodecamethylenbisacrylamide (DDMBA).

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