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ORAL PRESENTATIONS

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Chronic wounds treatment and regeneration via controlled release of antimicrobial peptides from chitosan-based multilayer patches

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Chronic wounds are a major social and economic problem, impacting both the healthcare system and millions of people's quality of life due to their increasing prevalence and cost [1]. Existing treatments, including mechanical/surgical cleansing and the administration of antibiotics (topical or systemic), are often painful, ineffective, or inadvisable, especially for patients with comorbidities that exacerbate the clinical picture. Therefore, it is crucial to find new strategies to overcome the existing hurdle associated with deep wound care. With the growing interest in biomaterials and regenerative approaches, many forms of dressings (membranes, foams, and hydrogels) have been investigated. They show great potential in wound healing, both for their properties and because they can be selected and blended to create composite materials with finely tuned physicochemical properties. Moreover, due to their composition and structure, biopolymer matrices can host therapeutics, such as antimicrobial peptides (AMPs), antibiotics or bioactive ions (Mg^{2+}, $Fe^{2+/3+}$, Cu^{2+}, Ag^{2+}, Zn^{2+}), and release them in a controlled manner directly at the infection site, thus avoiding antibiotic resistance's insurgence, often associated with antibiotic administration [3].

In this work, we took the innovative approach of conjugating LTX-109, a novel broad-spectrum topical antimicrobial peptide, with a biomaterial to develop an antimicrobial patch suitable to promote wound healing and skin regeneration. Specifically, we have designed a multi-layered patch with good biocompatibility and mimicry of the skin microenvironment, capable of administering the drug locally and assisting wound management from homeostasis to skin remodeling. The device was fabricated by the solvent casting technique using chitosan, which is widely used in wound healing [4], glycerol as plasticizer to contrast the brittle nature of the film, and tannic acid as cross-linker to control the chemical stability. Each layer was designed by choosing a different composition to obtain a tunable device: an upper protective layer with the function of shielding the wound from external contamination, followed by a medicated layer loaded with LTX-109, and a lower layer with multiple functions to modulate AMP release and provide regenerative stimuli.

Extensive characterization, including swelling ratio, water vapour transmission rate and degradation rate, showed that the patch meets the essential requirements for effective wound healing support, such as exudate absorption, maintenance of good O_2 and water permeation, biodegradability and biocompatibility, while HPLC analysis suggests that LTX-109 is released in a sustained manner, with full retention of its antibacterial activity, as indicated by the MIC values obtained against the reference bacteria.

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Eco-sustainable bio-polymeric biomedical HME filters: nature inspires the design of “artificial noses”

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For long-term mechanical ventilation, during anaesthesia or intensive care, it is crucial to preserve a minimum level of humidity to avoid damages at the respiratory epithelium and inspissation of secretions. HMEf, also noted as "artificial noses", are passive systems that maintain inspired gases at about the same conditions of healthy respiration, i.e., 32°C and relative humidity higher than 90%. This is in line with recommendations of the American Association for Respiratory Care that suggest an amount of moisture in the inspired gas (moisture output) higher than 30 mgH_2O/l.
Heat and moisture exchangers are intended to seize a portion of heat and moisture from the patient's exhaled air and release them into the inspired gas. Currently, the HME filters used in intensive care adopt the technology of almost 20 years ago, they are indeed constituted by synthetics materials, mostly polyurethane foams, or very chip but not performing materials, such as cellulose sheets. All of them suffer from limitations linked either to performance and filtration efficiency or to their inadequate antibacterial efficiency and sterilization methods. Also, durability is an important issue; in fact, most current HMEs are adversely affected by high temperatures (>32°C), humidity (>80%), and ultraviolet light. Furthermore, in times of global warming and diminishing petroleum oil reserves, replacing the employing of synthetic materials with biomasses has considerable economic and environmental value. Taking into account only the EU sales market standard HME generates a volume annually of 1.5 million of m^3 which needs to be burnt for disposal creating a big amount of CO2.
Therefore, living in a world where more and more efforts are being made to produce environmentally sustainable materials, an improvement in the development of HME filters is needed to create not only more effective devices but, particularly, to convert the entire HMEs’ production in a more eco-sustainable and circular-based one. Above all, in this work, we developed bio-HME through a green-chemistry process based on raw materials derived from food waste such as gelatin and chitosan. A biomimetic approach was followed to select polymers with the aim to reproduce the chemical structure of the glycoproteins representing one of the main components of mucus that are responsible to protect the respiratory system and to moisturize and warm the inhaled air. Polymers have been conveniently stabilized using a cross-linking agent and freeze-dried to obtain an aerogel with a specific aligned and porous morphology. The final HME, acting as an "artificial nose", accumulates the water vapor emitted by the patient during breathing, blocks any bacteria present and at the same time releases moisture during the inhalation phase, ensuring a rapid exchange process. Furthermore, the degradation test highlights as the filter results in stable during the usage time,

but in disposal conditions can easily degrade reducing heavily the disposable cost. In conclusion, the developed HME filter is featured by increased moisture output, lower pressure drop, affordable cost, antimicrobial efficiency, complete biodegradability, and are serializable by gamma rays. Concerning the shelf-life, the performance of our HME does not vary with temperature, UV light, and humidity; therefore, shelf life is remarkably longer and their packaging is simplified. These properties lead to the reduction of filter dimensions, waste treatment and handling costs, and offer a significant economic and social opportunity for the industry to meet the requirements imposed by the green economy and sustainable development.

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Collagen-based Materials with Wild Billbery Extract for Wound Healing

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Development of new composite materials with therapeutic applications is a major concern in the field of biomedical engineering. In this regard, natural polymers, such as alginate, chitosan, or collagen, have gained interest in the development of materials for tissue engineering due to their high biocompatibility and support in cell regeneration [1].

In this study, composite materials based on collagen for wound healing applications were developed using plant extract as source for bioactive compounds. Even though wild bilberry (*Vaccinium myrtillus*) fruits are greatly studied, leaves are also a valuable source of phytochemicals with biological benefits for human health, such as antioxidant, anti-inflammatory, antibacterial, antidiabetic and anticancer properties [2]. The polyphenolic extract obtained from bilberry leaves was rich in chlorogenic acid and rutin, evidenced through HPLC, which are known substances for their potential in preventing and assisting in various diseases [3,4].

The high porosity of mesoporous silica nanoparticles (MSN) allows hosting of a high amount of guest molecules; thus, the polyphenolic extract was embedded into MSN to increase the stability over time of bioactive components [5]. Furthermore, MSN surface properties can be tailored through functionalization. Carboxylic acid and proline moieties were grafted on the silica surface to modulate the interactions between guest molecules and MSN. The extract properties were tested before and after embedding into functionalized MSN, and the results showed improved properties when the extract was encapsulated in MSN. In terms of antibacterial activity, a reduction of the minimum inhibitory concentration on gram-positive and gram-negative bacterial strains was noticed after encapsulation. The encapsulated extract showed good cytocompatibility for normal human keratinocytes at concentrations up to 100 µg/mL and an anti-inflammatory potential on human keratinocytes. For wound healing applications, the marine-sourced collagen matrix showed promising results in wound healing test on HaCaT cell line, so it was used for the development of composite materials for topical application.

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Bringing microenvironmental complexity into *in vitro* cell cultures: 3D hydrogel-based systems for patient-specific B-cell lymphomas

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Advanced tumour models are striving to replicate living tissue functions in order to create an *in vivo*-like microenvironment. This drives the shift from cell monolayers to three-dimensional (3D) cultures since conventional two-dimensional (2D) methods fail to reproduce the diffusion gradients of nutrients, signalling molecules, and oxygen present in solid tumours. Lymphoma research has shown that immune and stromal cells' signalling molecules in the lymph node microenvironment may play a crucial role in cancer cell survival. Most functional studies on lymphomas grown in 2D cultures do not consider the effect of the immediate dilution of these signalling molecules. However, in 3D cell cultures, the diffusion behaviour is different, and released molecules can immediately act on neighbouring cells.

Biohybrid Gelatine-Methacryloyl (GelMA) hydrogels are a versatile tool for 3D cell cultivation due to their low immunogenicity, controllable mechanical properties, and high biofunctionality. GelMA allows cellular adhesion to its RDG motifs and enzymatic hydrogel remodelling, which can stimulate signalling pathways regulating cell migration, proliferation, and survival. The goal of this project is to create 3D *in vitro* lymphoma tumour models with higher complexity for personalised drug screening using patient-derived lymphoma and stromal cells. We developed a 3D GelMA-based gradient chamber that mimics the diffusion limitations present in solid tumours and used a biomolecular hypoxia reporting system to characterise oxygen gradients. With this model, personalised screening methods of higher complexity can be achieved.

Composite PLA/HA/GNP filaments developed for 3D printing

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Introduction: Currently, different biomaterials are combined to create novel, bespoke 3D bone repair solutions, some of which can be manufactured through the conversion of natural precursors [1] and can respond to economic variables like reduced production costs and waste materials reintegration [2]. This method was also involved to create feedstock materials for additive manufacturing processes (e.g., Fused Deposition Modeling (FDM) – requires the extrusion of the polymer as filaments). Therefore, the first crucial element to be established in the design and manufacture of efficient printable materials intended for various biomedical applications is the choice of appropriate precursor materials and was tackled for the first time in this study [3]. Further, based on the selected optimal precursor materials, a method for the composite filaments development, with improved surface and mechanical features [4], was proposed here.

Experimental methods: The prime materials, polylactic acid (PLA) and acrylonitrile butadiene styrene (ABS) were bought commercially. Bovine bone-derived hydroxyapatite (HA) and commercial graphene nanoplatelets (GNP) (grade C and M dimensions) were used as reinforcing materials. During the ad-mixing into the polymeric matrix, a tunable procedure was sought to modulate both the HA particles size (40 m, 100 m, and >125 m) and ratio (0-50%). Complementary physico-chemical and in vitro methods were applied for the characterization of the prime materials, followed by surface-volume characterization methods for the investigation of the extruded PLA/HA filaments. The biological experiments conducted at this stage sought to determine the optimal precursor materials in terms of biocompatibility.

Results and discussion: The FTIR-ATR investigations revealed only bands assigned to the characteristic vibrational modes, free of any impurities or other compounds, for all prime materials. Only the grade M type of graphene nanoplatelets retained their well-separated flake-like appearance. The final biological assessment allowed for the removal of ABS and GNP grade C samples due to their significant cytotoxic effects. Further, the SEM/EDS and micro-CT analyses of the composite filaments revealed the consistent internal distribution and arrangement of the HA particles as well as a sufficient adhesion at the PLA/HA interface. An enhanced wettability and gradual mechanical

takeover as the HA ratio increased, regardless of the particle size, further illustrated the benefits of evenly combining the natural PLA/HA composites.

Conclusions: The suggested technical approach enabled the selection of both the optimal prime materials and the ideal parameters for the synthesis of composite filaments intended for future applications in additive manufacturing and medicine.

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Plasma-Synthesized Pyrrole-Derived Polymer Evolution Implanted in Rhesus Monkey Spinal Cord Transection Model

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Introduction: In a spinal cord injury (SCI), nerve tissue is injured, resulting in paraplegia or tetraplegia depending on the level at which the injury occurred. Several studies have demonstrated the growth of neurons in cell culture on plasma-synthesized pyrrole-derived polymers (PPPy) as well as increased recovery of motor function after PPPy implantation in rat models of injury. In the process of transferring these advances to the clinic, it has been recommended to test in larger species, such as non-human primates (NHP), prioritizing in these studies the use of non-invasive techniques in order to assess the progression of the lesion with the treatments applied.

Experimental methods: The monomer used in the polymerizations was pyrrole. The polypyrrole was synthesized by the plasma polymerization method. FT-IR, XPS, TGA and morphological analyzes were performed.
This study was approved by the ethics committees of the IMSS, Project CAMINA A.C. and CI3M. The NHP were treated according with "National Institutes of Health Guide for the Care and Use of Laboratory Animals". Two NHP females (Macaca Mulatta) were used. They were selected based on their general appearance of health, mobility, vital signs, and blood chemistry. The NHPs underwent SCI, one was implanted with the polymer (RHI) and the other was injured only (RHC). MRI studies were performed with a 3.0 T whole body clinical MRI scanner. Three months after SCIT, subjects were sacrificed. Tissue surrounding the lesion was obtained. The samples were preserved for histological analysis.

Results and discusión: This work shows the monitoring of the evolution of TSCI in NHP by means of volumetric analysis (VA), fractional anisotropy (FA) and calculation of diffusion tensor tractography (DTT) around the lesion and the PPPy. Injury progression and PPPy status were analyzed up to three months after the day of injury using VA, FA, and DTT. VA preservation, AF recovery, and DTT restabilization were observed in RHI, in contrast to RHC. MRI-derived parameters are consistent with histology as well as demonstrated recovery of motor function.

Conclusion: The use of PPPy promotes functional recovery in an NHP SCIT model; as well as in the preservation of the tissue surrounding the area of the lesion.

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3D Bioprinted Scaffolds Based on Functionalised Gelatin and Sodium Alginate for Soft Tissue Engineering

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Introduction: Wound healing is a dynamic process and polymeric scaffolds were designed as promoters for wound closure and tissue development. Materials with various compositions and morphologies have with multiple functions have been tested and some of them successfully support the healing process of the wounded tissues [1]. In recent years, three-dimensional bioprinted (3D) technology has attracted a wide research interest in regenerative medicine due to possibility to obtain anatomical structures similar to physiological ones [2]. The basis of the bioprinting process is the bioink containing polymeric biomaterials, especially natural polymers or mixtures with synthetic polymers. Natural polymers are biocompatible and provide a favorable environment for cell attachment and proliferation [3]. This paper presents the obtaining of 3D bioprinted scaffolds using bioinks based on different combination between gelatin methacrylate (GelMa) and alginate methacrylate (AlgMa). The scaffolds were characterized and compared to establish the optimal bioinks composition and their applicability in soft tissue engineering.

Methodology: The polymers (gelatin, sodium alginate) were modified according to the protocol described by Camci-Unal [4], adding some changes to method. The methacrylation degree was calculated from FT-IR, NMR analysis, and analytical methods. For the preparation of bioinks, GelMa and AlgMa were mixed with photoinitiator, homogenized, and bioprinted (Cellink bioprinter), and freeze-dried for characterization. Bioprinted scaffolds were characterized for their structure, morphology (optical and SEM microscopy), swelling behavior in simulated physiological conditions, bioadhesion, *in vitro* degradability and *in vitro* citocompatibility.

Results: FT-IR and NMR spectroscopy data confirmed the methacrylic groups grafting onto polymeric chains. Likewise, FT-IR spectroscopy demonstrated the interaction between the polymer chains resulting crosslinked 3D networks. SEM microscopy demonstrated the formation of 3D structures with controlled porosity suitable for growth and proliferation of cells. The scaffolds are high swellable and degradable in presence of collagenase, necessary properties for tissue engineering applications. All materials intended to be used for medical applications must be tested by means of biocompatibility. On each material, cytocompatibility and morphological analysis were performed and values for cells viability over 90% were obtained. The cells maintained the normal shape of fibroblasts, and were uniform distributed.

Conclusions: The experiments confirmed the production of three-dimensional networks and emphasized the formation of porous materials with morphologies dependent on the ratio between polymers. The composition of the scaffolds influences pore sizes, degradation rates, and swelling ratio. The bioprinted scaffolds have pores that favor the diffusion of nutrients and cells development;

their degradation rate can be controlled by composition and bioprinting conditions. It has been found that the scaffolds do not have a cytotoxic effect, which property recommends these materials for future investigation as matrices for regenerative medicine.

Keywords: GELMA, Biopolymers, Hydrogels, Bioprinting, Tissue engineering.

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Atmospheric pressure plasma effects on 3D printing of model polymers

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Introduction: Surface science research focuses on surface modifications of polymers for improved surface adhesion, chemistry, or wettability, interaction with the human body or bodily fluids, and biological applications. Electrical gas discharges (plasmas) at atmospheric pressure are commonly employed in materials processing due to their flexibility[1-5].

Experimental methods: In this paper, electrical diagnosis and optical emission spectroscopy are used to describe a dielectric barrier atmospheric pressure plasma source operating in He. A quartz tube and two copper tape electrodes comprise the discharge setup, through which we employed He, at a flow rate of 2 SLM. A high voltage alternating current power supply drove the discharge. Three commercial polymeric filaments for 3D printing: acrylonitrile butadiene styrene, polyethylene terephthalate and polylactic acid, were plasma treated for 180 s. Atomic force microscopy, scanning electron microscopy, ATR-FTIR spectroscopy, X-ray diffraction, mechanical properties and static water contact angle (CA) techniques were used in the 3D printed polymer properties modification studies, after plasma exposure.

Results and discussion: At 48 kHz and up to 10 W mean power, the applied voltage on the discharge electrodes was roughly 10 kVpp, current intensity up to 15 mA, and an estimated average plasma energy of about 30 mJ. The global emission spectra, in the UV-Vis range contains helium lines, along reactive O_2 and N_2 species such as: NO, OH, N_2, N_2^+, O, that can produce surface modifications. We found increased hydrophilic effect of polymer foils after plasma treatment (from 59% for PLA to 76% for ABS). These results corresponding to a work of adhesion of water, Wa, increase from 71 mN /m (pristine value) to 131 mN /m for plasma treated PETG samples, from 91 mN /m to 127 mN /m for PLA, and from 68 mN /m to 139 mN /m for ABS. Moreover, morphology studies, via AFM and SEM revealed a smoother surface of plasma treated polymers, having lower root mean square roughness by ~20%. Tensile strength of the polymers, after plasma exposure prior to the 3D printing process, highlighted the increase strain of the plasma treated polymers versus the pristine ones. The benefit of plasma exposure was observed also through ATR-FTIR spectroscopy and via XRD diffraction on the polymer samples.

Conclusion: A correlation of plasma parameters, treatment time, morphological and chemical modification of plasma exposed materials was performed. The electrical and optical diagnosis of the studied plasma sources reveals the favorable operational parameters for proper surface treatment. Following studies on the morphology of surfaces, as a result of plasma treatments, the surfaces are much smoothed, with evenly distributed nanometric formations. The improved hydrophilic properties of the surface are reflected in an increasing of the surface energy after the plasma exposure. These results suggest that our plasma source is suitable for modifying polymeric materials as well as for future biomedical applications.

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Multifunctional Polymeric Nanocarriers of 'Difficult-to-Deliver' Active Substances for the Central Nervous System Disorders

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Neurodegenerative disorders are among the most lethal diseases of our civilization, and nowadays, the issue is superior due to the soaring mortality rates. Neurodegeneration includes ischemic stroke, characterized by a sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurologic function. The number of stroke cases and other neurodegenerative disorders, such as Alzheimer's and Parkinson's, sharply increases with age. Since our population is rapidly aging, prevention and treatment of stroke-related brain damage and neurodegenerative diseases, being still primarily unresolved problems of contemporary medicine, require new technologies for diagnostics and therapeutics. One of the critical limitations in treating such complex conditions is the inefficient delivery of neuroprotective substances through the blood-brain barrier (BBB). Most promising neuroprotectants are poorly water-soluble or even in-soluble substances, which makes them challenging to deliver. Their poor bioavailability in biological fluids, toxicity, low therapeutic concentration, non-targeted delivery, and undesirable side effects result in the low therapeutic effectiveness of neurodegenerative disorders treatment. Therefore, novel and effective drug delivery systems to the central nervous system (CNS) are strongly desired.
Our main objective was to develop a new strategy to deliver neuroprotective sub-stances by utilizing biocompatible theranostic nanocarriers, which can cross the blood-brain barrier (BBB) without imposing side effects on its normal function. The neuroprotectants-loaded theranostic nanocarriers were based on polymeric nanoparticles/nanocapsules (NPs/NCs). The polymeric NPs/NCs were prepared using nanoemulsion template methods, i.e., the spontaneous emulsification solvent evaporation method[1]. The technique allowed the preparation of two types of nanocarriers with a liquid core (stabilized by docusate sodium salt (AOT) and Poly L-lysine (PLL) complex) and a solid core (made of poly(caprolactone, PCL). A selected neuroprotective substance was encapsulated into the polymeric nanoparticles/nanocapsules. Such drug-containing polymeric nanocarriers were further modified/functionalized for theranostics using the layer-by-layer approach by creating multifunctional polyelectrolyte shells composed of poly-L-glutamic acid (PGA) and poly L-lysine or Gadolinium-labeled poly L-lysine (PLL-Gd), and PEGylated-PGA. The average size of obtained neuroprotectant-loaded theranostic nanocarriers of the core@shell structures was less than 200 nm. MRI confirmed the theranostic properties of such prepared core@shell nanocarriers. In contrast,

encapsulated neuroprotectants' biocompatibility and neuroprotective action were evaluated using cell viability and toxicity assays in the SH-SY5Y human neuroblastoma cell line. The developed neuroprotectant-loaded theranostic nanosystems may be considered promising platforms for CNS therapies.

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YOUNG SCIENTISTS' PRESENTATIONS

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3D Printable inks based on GelMA, Alginate and inorganic fillers

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One of the most modern approaches for tissue regeneration in regenerative medicine is 3D printing technique. Biopolymers-based inks must meet several requirements in order to be employed in 3D printing for biomedical purposes, including biocompatibility, shear tinning behavior, shape fidelity and mechanical stability of the printed scaffolds[1-4].
GelMA is a great material for additive manufacturing because of its outstanding morphological and mechanical stability as well as its customizable mechanical capabilities. The biopolymer can be crosslinked by a flexible photocuring procedure employing biocompatible photoinitiators thanks to the grafted methacryloyl groups; UV light offers good temporal and spatial control over the crosslinking mechanism.
Due to its present biocompatibility and inexpensive cost, alginate is also frequently employed in regenerative medicine. On the other hand, nanofillers are now being used to improve rheological and biological properties.
The primary objective of this study was to develop effective materials that are appropriate for 3D printing process and that can be employed further in tissue regeneration and regenerative medicine. In order to achieve these objectives, GelMA or Alginate was used as the biopolymeric matrix, and clay or hydroxyapatite as inorganic nanofillers.
Nanocomposite-based scaffolds were characterized structurally (FTIR), morphologically (SEM, Micro CT), and biologically.
The 3D printed developed nanocomposite structures are highly recommended to be employed as scaffolds with the appropriate characteristics for prospective biomedical applications.

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Design of Electrospun and 3D-printed Scaffold co-loaded with Therapeutic Agents for Antibacterial Wound Dressings

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The research work introduced an efficient solution for antibacterial wound dressings by engineering drug and prodrug-co-loaded bicomponent scaffold, using the strategy of combining electrospinning and 3D-printing technologies[1-3]. The outer component was constituted by a chitosan (CS) electrospun membrane loaded with indomethacin-based prodrug (pIMC), which served as support for printing the inner component, a gelatin methacryloyl (GM)/ sodium alginate (SA) 3D hydrogel loaded with tetracycline hydrochloride (TCH).

In order to obtain the bicomponent scaffold, firstly it was necessary the design of pIMC-containing CS nanofibrous membrane (F/pIMC) by electrospinning as outer component, and secondly, the design of TCH-loaded GM/SA hydrogel (H/TCH) by 3D-printing and its double crosslinking (GM photopolymerization and ionic crosslinking of SA), as inner component. The assembling of the two components was achieved by printing the hydrogel onto the surface of nanofibrous membrane.

SEM micrographs underlined both the nanofibrous architecture of non-crosslinked and crosslinked electrospun membranes, and the porous microstructure of 3D-printed scaffolds, as well as the joining of the two components in the final bicomponent scaffold. The study of drugs release profiles revealed that both F/pIMC and H/TCH released the therapeutics in a controlled and sustained manner when they were in the presence of enzymes. According to *in vitro* cytocompatibility evaluation (MTT assay), the HeLa cell culture exhibited a good viability in the presence of bicomponent scaffold, which suggests that this could promote HeLa cells adhesion and proliferation. The bicomponent scaffold also manifested an excellent antimicrobial activity against *E. coli* and *S. aureus* bacterial strains.

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Designing Novel High-performance Asymmetrical Benzoxazine Monomers through Green Chemistry

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Benzoxazine resins have encountered a tremendous progress along time, being one of the most representative classes of thermoset polymers due to their outstanding thermal, chemical, and mechanical properties and playing a leading role in the development of cutting-edge technologies, coatings, and microelectronics[1].

Over the last decade the design of benzoxazine thermoset, became more oriented toward green chemistry and thus biomass resources replacing the conventional phenol, primary amine and formaldehyde were involved in the Mannich condensation reaction[2]. The versatility of this polymeric materials represents one of the central assets around whom desirable properties can be tailored. Tyramine, a biogenic amine obtained by decarboxylation of tyrosine represent a valuable and abundant amino acid derivative that can be isolated from food. When it comes to benzoxazine chemistry, tyramine is an important resource due to the fact that it possesses two functional groups that constitute the fundamental substrate for the oxazine ring formation.

The aim of this research paper was to develop dibenzoxazine monomers by exploiting the complex functionality of tyramine which can act both as phenol and primary amine in the Mannich condensation reaction and to design new bio-based polybenzoxazine thermosets with superior thermo-mechanical properties through a facile and greener synthesis procedure. Herein, starting from renewable resources such as eugenol, sesamol, furfurylamine and tyramine, new benzoxazine monomers were synthesized and purified in ethanol as green solvent.

The molecular structure of tyramine based benzoxazine monomers was characterized by FT-IR and H NMR. The thermally activated ring opening polymerization was monitored by differential scanning calorimetry (DSC) and the curing kinetics were investigated by the Kissinger and Ozawa methods. The crosslinked polybenzoxazine networks showed very high thermal stability with a T_{d5} around 400 °C and high mechanical properties. The outstanding performance of the synthesized polybenzoxazines highlights their potential applications in the design of highly thermally stable polymeric materials.

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Development of bioinspired 3D printable nanostructured formulations for bone tissue regeneration

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Bone tissue regeneration presents numerous challenges in the field of regenerative medicine, due to limitations associated with the conventional approaches employed when the natural healing abilities of the bone are exceeded. 3D printing technologies combined with multimaterial formulations raise a transformative approach for bone tissue regeneration, allowing the development of custom-made scaffolds with precise architectures and compositions for personalized therapeutic strategies.

Bioinspired nanostructured multimaterial formulations were developed for 3D printing and bioprinting, based on a TEMPO-oxidized cellulose nanofibrils gel, methacryloyl gelatin and alginate. The hydrogel matrix was loaded with magnesium-doped hydroxyapatite nanoneedles, promoting osteoconductivity, and with carboxylated nanodiamond particles, as nanoplatforms for the stimulation of cellular attachment and reinforcing agent. Nanocomposite formulations were developed stepwise, predefining the interactions between the components of the multimaterial formulations (Figure 1).

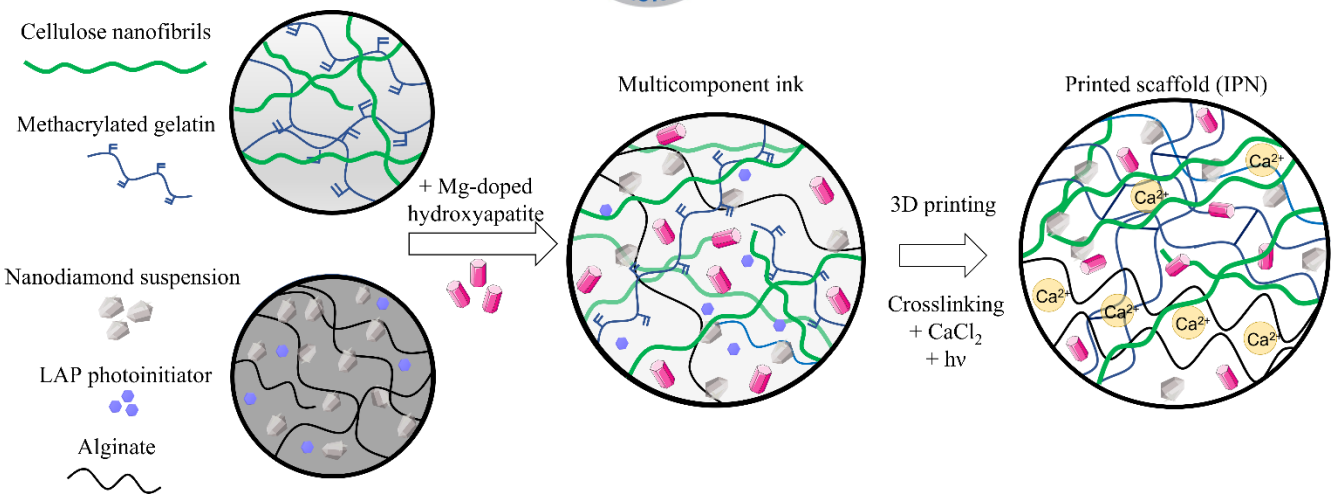

Figure 1. Predefining interactions between multimaterial formulations' components.

The rheological behavior of the components was studied both individually and in various associations to evaluate their suitability for 3D printing applications. Further, the multimaterial composition was 3D printed using two different equipments, showing high process reproducibility. The morpho-structural characterization of the printed objects was performed through SEM/EDS and micro-CT. The scaffolds were evaluated in terms of dimensional stability, swelling kinetics, gel fraction and preliminary degradation. The results are consistent with soft hydrogels' behavior, demonstrating potential for the multimaterial formulation's use in 3D printing applications of hydrated micromediums that can potentially promote and sustain bone tissue regeneration.

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Screening of Carboxylated Nanodiamonds Interactions with Porcine Gastric Mucin and its Methacryloyl Derivative

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Introduction: Nanodiamonds possess the greatest cytocompatibility among all carbon nanostructures, being suitable for designing composite biomaterials [1]. Mucin, the main glycoprotein found in mucus, is a promising candidate for biomaterials synthesis, being characterized by a very complex bottlebrush-like structure rich in various functional groups [2].
Experimental methods: The present study presents the evaluation of (1) porcine gastric mucin (PGM) – carboxylated nanodiamonds (NDs) interactions and (2) methacryloyl mucin (MuMA)– NDs interactions. To this end, a Quartz Crystal Microbalance with Dissipation Monitoring (QCM-D) study was performed. In short, PGM was adsorbed onto a gold sensor surface, on top of which NDs were circulated for 15 minutes with a flow rate of 0.1 ml/min and let to interact for another 15 minutes. Then, the unbound species were washed, and a second layer of protein was circulated for 15 minutes with a flow rate of 0.1 ml/min and let to interact for another 15 minutes, after which a final washing step was performed. The frequency decreases after each step suggesting that every layer was formed through stable interactions. The influence of NDs on protein structure was evaluated through circular dichroism (CD) and Fourier-transform spectroscopy (FTIR).
Results and discussion: Results showed that both glycoproteins were adsorbed onto the sensor surface as indicated by frequency decrease with higher adsorption recorded for PGM. The addition of NDs-COOH leads to a higher decrease in frequency and to an increase in dissipation suggesting that NDs interact with protein probably with the rearrangement of protein macromolecules. Up to the end of the QCM-D measurement, the mass continuously increased, and the rigidity of the layer decreased. When compared, all results showed more pronounced interactions of the nano-species with PGM when compared with methacryloyl PGM without the denaturation of glycoprotein structure in either case. Moreover, FTIR spectra and QCM-D graphs have shown that NDs block UV-photopolymerization.

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Surface-functionalized cellulose acetate membranes with enhanced biomineralization ability

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From all the existing membrane modification techniques, surface functionalization by covalent immobilization is the most convenient one because it allows a highly selective binding and prevents the leeching of the immobilized compound into the surrounding aqueous environment. During covalent immobilization, stable bonds are formed between the functional groups of the substrate and the functional groups of the active compound [1]. In this study, the surface of commercial cellulose acetate membranes was functionalized with 4′-aminobenzo-15-crown-5 ether, using a covalent bonding approach. The purpose of this study was to develop a novel generation of cellulose-based membranes with applications in the biomedical field, particularly in osseointegration, by functionalizing the surface of cellulose acetate with 4′-aminobenzo-15-crown-5-ether (AB15C5) using ethanolamine (EA) as modification agent and glutaraldehyde (GA) as linker molecule. Crown ethers are macrocyclic polyethers containing a central cavity lined with oxygen atoms where they can accommodate positive metal ions or a variety of neutral and ionic organic species. The metallic cations are stabilized by the interactions with the lone pairs of electrons on the surrounding oxygen atoms forming a host-guest complex [2]. The proposed reaction mechanism was confirmed by XPS analysis while the presence of the functionalization agents in the membranes structure was showed by ATR FT-IR spectra. The effects of the functionalization process on the morphology, thermal and mechanical properties of the membranes were studied by SEM, TGA and tensile tests. The obtained results revealed that the cellulose acetate membranes were successfully functionalized with crown ether and provided a good understanding of the interactions that took place between the polymer and the functionalization agents. Moreover, promising results were obtained during the Taguchi biomineralization studies. SEM images, EDX mapping and XRD spectra indicating that the CA-AB15C5 membranes have a superior Ca^{2+} ions retention ability, this causing an accentuated calcium phosphate deposition on the modified polymeric fibers, compared to the neat CA membrane.

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combined with stimuli responsive drug delivery—a new generation of polymeric membranes for advanced biomedical applications within PNCDI III. Madalina Oprea kindly acknowledges University Politehnica of Bucharest by the project “Pregătirea doctoranzilor şi cercetătorilor poStdoctorat în vederea dobândirii de coMpetenţe de cercetARe aplicaTivă-SMART”, MySMIS 2014 153734

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Polysaccharides based drug delivery system for the encapsulation of ketoprofen

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Biomaterials, in a collaborative manner which includes different fields like engineering, chemistry, physics, biology, and medicine, have been use in producing advanced drug delivery systems for decades[1].Various ways have been developed toward obtaining and optimizing different drug delivery systems for numerous kind of drugs, enzymes or proteins. By selecting the proper drug delivery system, we can improve drug action in the body, by increasing the efficiency of the treatment and reducing side effects of the drug [2]. Manny biopolymers have been used to develop new materials to release therapeutics due to their non-toxicity, biocompatibility, biodegradability, mucoadhesive properties and low price. Polysaccharides such as alginate, pectin, chitosan, and k-carrageenan are widely used as biomaterials in pharmaceuticals, in the food industry, and in tissue engineering because of their properties [3, 4].

The aim of our work is to formulate polysaccharide-based interpenetrating network beads obtained by ionotropic gelation of k-carrageenan and sodium alginate for the encapsulation of ketoprofen to provide an improved drug release. The bi-component particles were characterized thought FT-IR spectrometry and UV-Vis spectroscopy was used to assess the encapsulation efficiency of the biomaterial and the drug release kinetic of ketoprofen in simulated body fluids. Also, the swelling tests were performed to highlight the behavior of the materials in simulated gastric fluid and in simulated intestinal fluid.

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Chemical Modification of Chitosan Towards a Wider Purpose Spectrum in Osteochondral Tissue Engineering Applications

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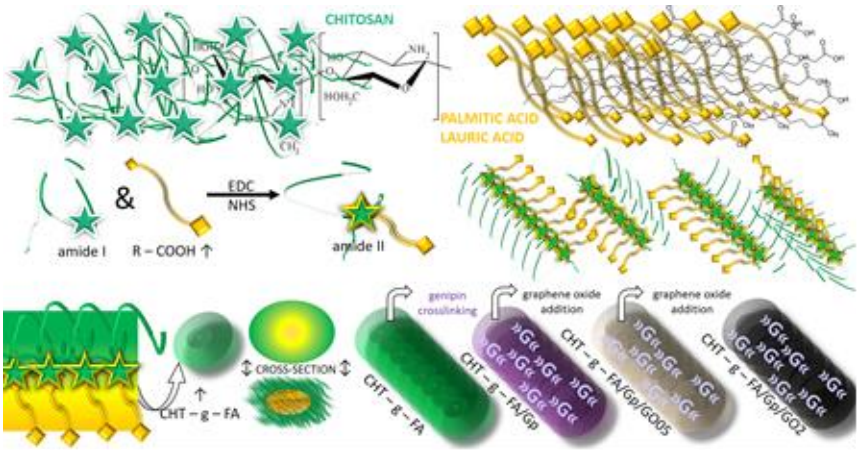
We present the design of new graphene oxide composites based on chitosan modified with fatty acids, that resulted in amphiphilic structures with increased morphological and structural variability. Chitosan-fatty acid derivatives are synthesized via N,O-acylation of chitosan with palmitic and lauric acid. Obtained co-polymer assembled in core-shell-like items were further crosslinked with genipin and composited with graphene oxide. The FTIR technique was used to demonstrate the modification and to chemically characterize novel materials. DLS, SEM and contact angle measurements were used to investigate the surface attributes of the samples, which revealed that hydrophobic components linked into chitosan macromolecules resulted in an increase in both surface roughness and water contact angle values. Nanoindentation tests highlighted notable durotaxis gradient in-depth due to polysaccharide / fatty acid self-organization and also as a result of graphene sheets embedment. Graphene oxide containing materials were more stable in phosphate buffer saline and lyzozime incubation and swelled less due to additional physical interactions developing among the composited building blocks. Finally, preliminary viability, cytotoxicity and inflammatory response tests revealed that all chitosan-fatty acid composite derivatives were promising while in vitro protein adsorption assay indicated a potential antifouling activity of the composites. Our findings show that the proposed synthesis, notably the graphene oxide/chitosan-fatty acids composite derivatives, have the potential to be used as risk-free durable and stable substrates with heterogeneous architecture in biomedical applications.



Conceptualization of the experimental design involving the synthesis of copolymer and its derivatives

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POSTER PRESENTATIONS

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3D Bioprinting of CNFs-Based Bioinks for Tissue Engineering

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Introduction: Over the years, the number of patients suffering from various injuries and degenerative processes has constantly increased. The development of additive manufacturing and 3D printing techniques supported the progress of tissue engineering and regenerative medicine, allowing the fabrication of 3D printed scaffolds with an extremely complex structure, in a repeatable and precise manner. Different nanocomposites incorporating functionalized nanomaterials were proposed as 3D scaffolding systems for bone tissue reconstruction. Cellulose nanofibrils (CNFs) have a positive impact on the printing process, conferring shape fidelity and printing uniformity, but also on cell viability and proliferation. On the other side, polyhedral silsesquioxanes (PSS) nanoparticles have recently received substantial attention, due to their ability to promote chemical interactions and cell growth. Thus, the aim of our research was to investigate the capacity of multicomponent hydrogel bioinks based on CNFs and two distinct types of PSS (non-functionalized and 1-methacrylated) enriched with human bone morphogenetic protein 2 (BMP-2) to support preosteoblasts viability and proliferation.

Experimental methods: The cross-sectional morphology of the nanocomposites was recorded through scanning electron microscopy (SEM) micrographs. Murine preosteoblasts from MC3T3-E1 cell line were embedded in the material ink forming a bioink that was further printed. The 3D bioprinted scaffolds were maintained in complete culture media for 7 days in standard conditions (37°C, 5% CO_2 and humidity). The biocompatibility evaluation was assessed after 2 and 7 days of cell culture. Cell viability and proliferation were measured by quantitative MTT assay and cytotoxicity was evaluated using LDH assay. The ratio between live and dead cells was assessed by fluorescent label with Live-Dead assay.

Results and discussion: Representative SEM images of the nanocomposites showed that all samples exhibited large interconnected pores desirable for cell growth and migration. The results of the biocompatibility assessment performed on cell-laden 3D printed scaffolds revealed that the combination of CNFs and PSS provides an appropriate environment for cell growth and proliferation since high viability rates were determined for all composites after 7 days of incubation in standard conditions. The presence of PSS nanoparticles promoted higher proliferation rate compared to the PSS- free 3D bioprinted scaffold. Moreover, the addition of the osteoinductive agent BMP-2 increased cellular activity and provided proper conditions for favorable cell distribution, viability and proliferation.

Conclusions: 3D printing became an important research field which aims to obtain 3D-bioprinted scaffolds with appropriate mechanical and biochemical properties. The association between CNFs, PSS and BMP-2 exhibited positive influence on the viability and proliferation of embedded murine preosteoblasts during the 3D bioprinting process, demonstrating that the bioinks developed in this study are viable candidates for bone tissue engineering applications.

Acknowledgment: This research was funded by the Romanian Ministry of Education and Research, CNCS-UEFISCDI, project number PN-III-P1-1.1-TE-2019-0787, within PNCDI III.

New Polymeric Architectures Based on Methacrylated High Oleic Sunflower Oil and Compatible PEG Derivative

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In an age with more and more concerns about pollution, exploring renewable feedstock represents the key factor for a low environmental footprint[1]. Using vegetable oils (VO), with various advantages and versatile chemical structure as alternative to conventional petroleum-based feedstock represents an excellent sustainable way to produce new chemicals and innovative materials for basic or more complex applications[2].

To overcome the VO disadvantages associated with their hydrophobicity or weaker mechanical properties, rational functionalization or combining with other components enables adequate modulation of the final properties for the envisaged application[2,3].

The aim of the current study was to obtain and evaluate new polymeric architectures starting from two high oleic sunflower oil (HO-SFO) monomers: methacrylated (MA-HO-SFO) and methacrylated PEGylated (MA-HO-SFO-PEG). Both oil-based monomers were obtained within this study, Figure 1 presenting the involved synthesis route.

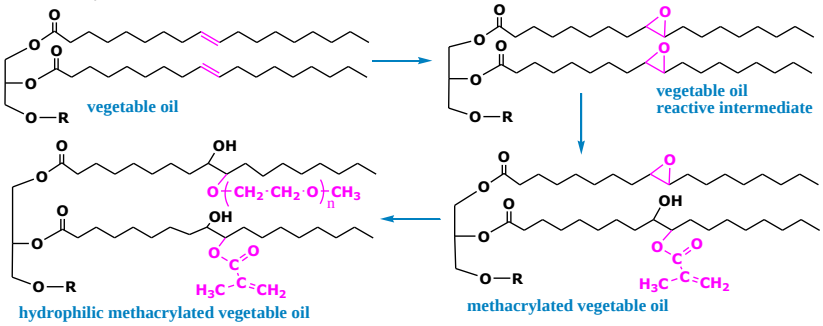

Figure 1. Functionalization strategy to obtain HO-SFO-based monomers

Fabrication of the new sustainable polymeric materials involved both derivatives of HO-SFO, in combination with different amounts of compatible polyethylene glycol dimethacrylate (PEG-DMA), as strategy to obtain some valuable properties for biomedical applications. Bulk photo-polymerization in mild conditions (visible light, room temperature, cell-friendly initiators) was employed to obtain oil-based monoliths, based on the schematic experimental protocol from Figure 2.

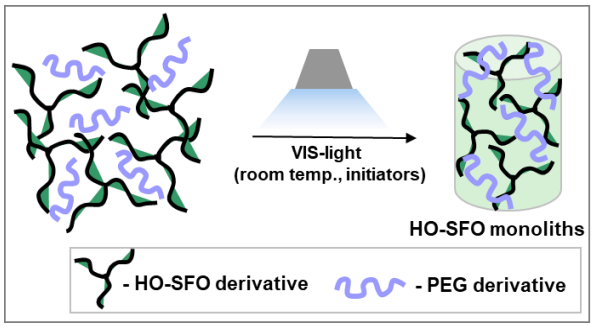

Figure 2. Experimental protocol to obtain polymeric architectures based on HO-SFO

The influence of PEG-DMA amount on the HO-SFO-based networks was studied and certain properties at the intersection of material performance and biomedical application were investigated (structural characterization, crystallinity degree, PBS absorption, morphology). The obtained results will be presented.

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Skin-like polymer hydrogels for wearable electronic devices

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Skin-like electronics are progressing rapidly to realize a variety of applications such as wearable sensing and soft robotics. Soft biomimetic electronic devices primarily include an electronic skin (e-skin) capable of implementing various wearable/implantable applications such as soft human–machine interfaces, epidermal healthcare systems, and neuroprosthetics owing to its high mechanical flexibility, tissue conformability, and multifunctionality[1]. Hydrogels, as soft biomaterials, have been explored intensively for skin-like electronic utilities due to their unique features such as softness, wetness, biocompatibility and ionic sensing capability[2].
In this study, we report a new kind of double-network hydrogel based on polyacrylamide and alginate and graphene oxide exhibiting high stretchability with potential applications in the fields of the biosensor,
wound dressing, tissue engineering, and biosensor (Fig. 1).

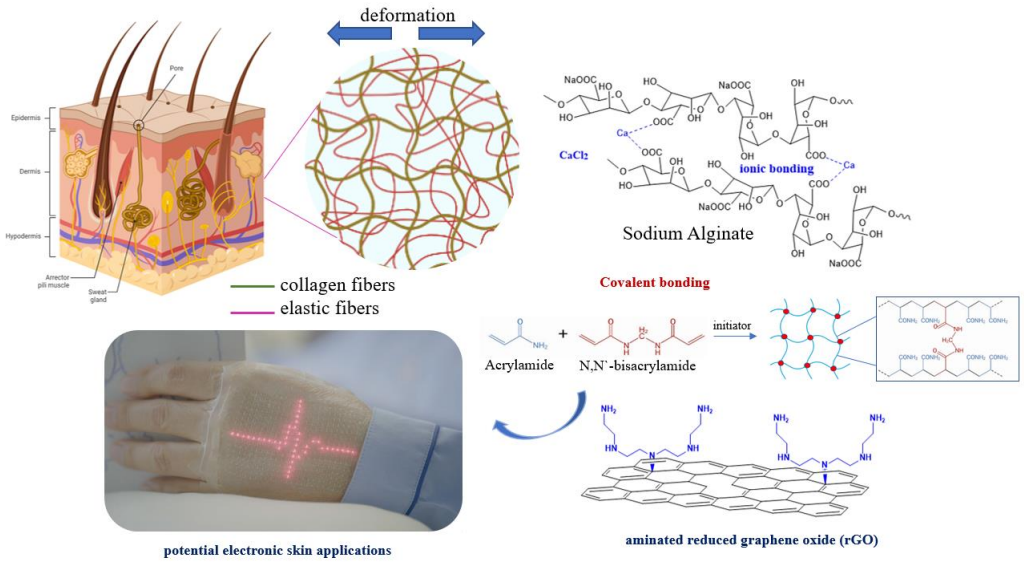

Fig. 1. Synthesis of the composite hydrogel based on polyacrylamide, and crosslinked alginate reinforced with aminated graphene oxide

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Investigation of laser-polymer film interactions by time-resolved imaging

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In recent years, significant advancements have been achieved in comprehending polymer ablation, whether in terms of novel material development or the understanding of ablation mechanisms related to emerging laser systems. However, there exists a substantial disparity between the progress made in developing new applications and the availability of research tools. Consequently, gaining insight into the interaction between lasers and polymers is crucial to selecting the appropriate laser source for specific applications and fully harnessing the potential of lasers.

Lately, both the scientific and industrial communities have displayed heightened interest in laser-induced forward transfer (LIFT) as a tool for additive manufacturing. In LIFT, a laser pulse is focused at the interface between a donor substrate and a thin film. The rapid absorption of the laser beam causes a small portion of the donor material to propel onto the receiving substrate. When transparent donor materials are used, a dynamic release layer (DRL) can be introduced between the donor substrate and the film to enhance laser pulse absorption and subsequent material propulsion.

Thus, investigating the interaction between the laser, substrate, and polymer bond is crucial for controlling the LIFT process. This interaction generates pressure loading based on the laser intensity profile and entails the propagation of induced shock waves within the donor film.

Simulation results obtained using the hydrodynamic Helios code are compared to shadowgraphy experiments involving the interaction of a nanosecond (ns) laser beam with a photosensitive polymer employed as a DRL. The velocity calculated through simulations demonstrates good agreement with experimental results, accurately predicting the response to propagating shock waves.

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Peptides-Functionalized Micro/Nanospheres for the Treatment of Respiratory Infections

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In recent years, inflammatory lung diseases have started to become a major health problem worldwide, as they can be caused by infections with viruses, bacteria, parasites or fungi. In this context, drug carriers for pulmonary applications have become a popular topic and various micro and nanoparticle systems have been investigated, including liposomes, micelles, dendrimers, micro/nanospheres or polymeric micro/nanocapsules [1]. The objective of the present study consisted in the preparation of biocompatible and biodegradable dexamethaseone-loaded micro/nanospheres functionalized on the surface with two specific peptides that can be used as pulmonary drug delivery systems.

Micro/nanospheres (M/NSs) based on chitosan carboxylate (CMCS) and poly(vinyl alcohol) (PVA) were prepared by inverse emulsion (W/O). The originality of this study is given by the fact that the preparation method does not involve the use of chemical crosslinkers, potentially toxic. Instead, the esterification of the carboxylic groups of CMCS with the hydroxyl groups of PVA and amidation of the remaining amino groups of CMCS with its carboxylic groups is initiated by an activator agent, 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM). Another original aspect of this study is related to the functionalization of the M/NSs with two specific peptides, CGSPGWVRC and indolicidin, as efficient ligands for active targeting of both alveolar capillary endothelial cells and bacterial cells responsible for pneumonia. The peptides were conjugated by amidation of their amino groups to CMCS.

The obtained M/NSs were characterized from a physico-chemical point of view and their structure, size, shape and swelling behavior were investigated. *In vitro* drug loading and release as well as biological properties were also studied.

The amidation reaction between CMCS and peptides was confirmed by FTIR spectroscopy using a single reflection ATR accessory QATR-S of a Shimaszu IRSpirit spectrometer. The reaction between the hydroxyl groups of PVA and the carboxylic groups of CMCS in the presence of DMT-MM was demonstrated also by FTIR spectroscopy.

The average diameters of the obtained spheres were analyzed using the laser light diffractometry (DLS) technique (Zetasizer Nano ZS from Malvern Panalytical). The spheres morphology was determined by scanning electron microscopy (SEM) (Quanta 200 Scanning Electron Microscope produced by FEI Company). The average diameter was between 570 nm and 1300 nm. A direct

correlation was noticed between the particle's sizes and the amount of chitosan. The obtained particles have a well-defined spherical shape and a smooth surface.

In vitro release studies were performed using a dissolution apparatus (Dissolution Apparatus 708-DS) equipped with a sampling station (Sampling Station, 850-DS). The release of the drug in the weak basic medium that mimics the blood environment was influenced by the swelling degree of the particles.

Assessment of biological properties demonstrated that the obtained particles can be included in the category of hemocompatible materials, producing lysis of only up to 1.4% of red blood cells at the highest studied concentration. It was also found that the adsorption efficiency of bovine serum albumin and the mass loss in the presence of lysozyme for the tested samples was influenced by the initial amount of chitosan in the particles.

These obtained results demonstrate that the obtained carriers can be a safe alternative for the treatment of pulmonary infections and therefore further and more detailed *in vitro* and *in vivo* tests will be carried out.

Acknowledgements: This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P4-ID-PCE-2020-2009, within PNCDI III.

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Impedimetric Label-Free Biosensor Based on Reduced Graphene Oxide and Gold Nanoparticles for Detection of Oligonucleotides

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The progress made in medicine and nanotechnology paves the way for the development of innovative devices. Our objective is to develop a portable device capable of detecting nucleic acids at the point of care. To achieve this, we propose an electrochemical platform that incorporates reduced graphene oxide (RGO) and gold nanoparticles (AuNPs). For the detection platform, we used screen printed carbon electrodes (SPCEs) as a foundation. These electrodes were modified by electrochemically reducing graphene oxide and functionalizing them with AuNPs through cyclic voltammetry (CV) technique, resulting in AuNPs-RGO/SPCE. To enable detection, a bioreceptor in the form of a single-stranded DNA probe was immobilized onto the electrode surface through physical adsorption. Subsequently, the functionalized SPCEs were exposed to the complementary single-stranded DNA target, leading to the formation of double-stranded DNA through a hybridization event that needs to be identified.
The immobilization of gold nanoparticles on the electrode surface was confirmed through scanning electron microscopy (SEM), which allowed for the morphological characterization of the modified structure. Additionally, the structural characterization of the functionalization process was conducted using X-ray photoelectron spectroscopy (XPS), which confirmed the successful functionalization with AuNPs. Furthermore, the electrochemical properties of the modified electrodes were examined after each modification step. This investigation involved employing cyclic voltammetry and electrochemical impedance spectroscopy (EIS) in a 0.1 M KCl solution containing the $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$ redox pair (1:1). The modification of RGO/SPCE with gold nanoparticles resulted in improved electrical conductivity, a crucial characteristic for developing a biosensor with enhanced sensitivity. Moreover, the binding of the target DNA to the bioreceptor was determined by monitoring changes in the electrochemical signal. Specifically, the measurement of charge transfer resistance using EIS and corroborated by CV was utilized to assess the interaction between the target DNA and the bioreceptor, thus confirming the results.

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Reduced graphene oxide hybrid with gelatin for multimodal cell imaging

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In the field of cellular imaging, graphene oxide (GO) has emerged as a promising candidate due to its low toxicity1. Also, reduced graphene oxide (rGO) has the potential to be highly biocompatible with living cells, particularly when combined with a suitable polymer. In this context, we sought to develop a hybrid contrast agent that would efficiently combine the high surface area and the versatile surface functionalization of rGO with increased biocompatibility and biodegradability of the biopolymer. To achieve this, herein we turned to gelatin, a biopolymer that is known for its versatility and biocompatibility.

Concretely, to synthesize our stable contrast agent, we first prepared GO using the Hummers protocol2. After mixing the GO suspension with the gelatin solution, we reduced the GO using a green reduction process with Ascorbic Acid (AA). To confirm the successful reduction process and the attachment of the gelatin to the rGO sheets we employed multiple spectroscopic analyses such as FTIR, Raman, UV-VIS, Fluorescence and X-ray Diffraction (XRD) and Thermogravimetric Analysis (TGA) investigations. In addition, the structure and morphology of the resulting hybrid rGO-GEL were investigated by Scanning-Transmission Electron Microscopy (STEM).

Having in mind our final purpose, the cytotoxicity of the hybrid rGO-GEL inside melanoma B16-F10 cells was also assessed by MTT test, confirming its biocompatibility. Finally, the intracellular tracking after 24h of treatment was performed by non-invasive Confocal Fluorescence Microscopy as well as Enhanced Resonance Raman Scattering imaging. In conclusion, we have successfully synthesized a stable and biocompatible rGO-GEL hybrid as a suitable contrast agent candidate for cellular imaging of interest.

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The Use of Graphene Oxide and Montmorillonite Structures as Active Reinforcement for Vegetable Oil-based Polymeric Materials

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Introduction. The strategy of using natural resources to fabricate polymeric materials is more and more researched, being a great alternative for the extensive use of non-renewable petrochemicals. In this context, conventional epoxy resins, the most used components in various hi-tech industries, are intended to be replaced with their sustainable counterparts, derived from vegetable oils (VO)[1]. However, polymeric materials based on the epoxy derivatives of VO do not express remarkable mechanical properties, due to their chemical structure with long aliphatic chains, reinforcement strategies being the most suitable ones when this shortcoming must be surpass[2].
The current research work was focused on the development of bio-nanocomposites based on epoxidized vegetable oils (EVO) reinforced with different nano structures.

Experimental. EVO-based nanocomposites were formulated using graphene oxide (GO) and montmorillonite (MMT) as active fillers, targeting high mechanical features and fire-resistant properties for the final materials. Thermal curing processes were involved, in the presence of selected curing agents.

Results. The thermomechanical properties of the synthesized nanocomposites were evaluated and correlated with the structure of the nanofillers by dynamic mechanical analysis (DMA), tensile testing, and thermogravimetric analysis (TGA). The influence of the chemical particularities of each hybrid nanomaterial over the curing process of the polymeric matrix was evaluated through differential scanning calorimetry (DSC).
The assessment of structure-properties correspondence for bio-based epoxy networks reinforced with MMT/ GO hybrids was critical to further apply as thermoset materials in different domains.

Conclusion. The assessment of structure-properties relation for bio-based epoxy networks reinforced with MMT/ GO hybrids was established as key parameter for the fabricated bio-based materials, related to the potential applications.

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New Polydimethylsiloxane (PDMS) modified interfaces: physical-chemical characteristics and *in vitro* effect on cell behaviour

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One strategy to develop new and more efficient biodevices used as implants is based on surface physical-chemical modifications in order to prevent undesired biological responses[1, 2].
The physical-chemical characteristics of the newly proposed Poly(2-methacryloyloxyethyl phosphorylcholine) (pMPC) functionalized scaffold obtained by Matrix-Assisted Laser Evaporation (MAPLE) method[3] were evaluated by Scanning Electron Microscopy, Atomic Force Microscopy, Contact angle, Surface energy, Fourier Transform Infrared Spectroscopy and X-ray Photoelectron Spectroscopy. The assessment of adhesion, proliferation and morphology of cells grown on the functionalized Polydimethylsiloxane (PDMS) surfaces was performed *in vitro*, using human macrophages and fibroblasts, cells involved in foreign body reaction.
The results obtained after evaluation of the physical–chemical properties of the new coatings revealed that the MAPLE technique proposed has the advantage of achieving homogeneous, stable and moderate hydrophilic thin layers onto hydrophobic PDMS. Moreover, this approach does not require any pre-treatment, therefore avoiding the major disadvantage of hydrophobicity recovery. Biological investigation evidenced the reduction of the adhesion and proliferation of human macrophages by ~50% and of human fibroblast by ~40% on the modified surfaces of PDMS compared to unmodified scaffold, thus circumventing undesired cell responses such as inflammation and fibrosis.
All these highlighted the potential for the new PDMS interfaces obtained by MAPLE to be used in the biomedical field to design PDMS-based implants exhibiting long-term hydrophilic profile stability and better mitigating foreign body response.

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New bio-hybrid structures based on natural polymers and silicon compounds for tissue engineering

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Bone tissue loss due to trauma or related diseases leads to a significant decrease of the quality of life for patients and conventional approaches, based on the use of autografts and allografts, raise problems related to availability. Therefore, the need for developing novel approaches for tissue engineering is emphasized[1].

In this study we present the synthesis of scaffolds based on pectin, gelatin and silicon compounds as a solution to the mentioned issue. Type B gelatin from bovine skin and high methoxyl pectin from citrus peel were used to obtain the scaffolds. In addition, the samples were reinforced with inorganic POSS nanostructures: (i) having no functional groups or (ii) with one epoxy group attached on the cage. All the samples were cross-linked with 3-glycidoxypropyl-trimethoxysilan (GPMTS) and half of them were supplementary set through a bioinspired sugar-acid gelation process.

The results of the swelling study showed a higher swelling degree for the samples cross-linked only with GPTMS compared to those double cross-linked, proving that the pectin gelation in the presence of sugar was efficient and formed numerous interactions between the polymer chains.

Scanning electron microscopy (SEM) images indicated that all the samples showed uniform and interconnected porosity, with pore diameters that allows the access of osteoblast cells. In addition, the energy dispersive X-ray analysis (EDAX) indicated that all samples presented a high concentration of silicon. The uniform distribution of the silicon in the polymeric matrix was confirmed by the EDAX mapping images thus proving the effectiveness of the sonication process.

The MTT results exhibit higher cell viability for the double cross-linked samples, the highest viability being recorded for the double-crosslinked sample reinforced with POSS0. Additionally, the LDH assay confirmed the samples biocompatibility. The obtained samples displayed a morphology that allowed the diffusion and attachment of osteoblasts (Fig 1), thus being suitable for use in the regeneration of the bone tissue.

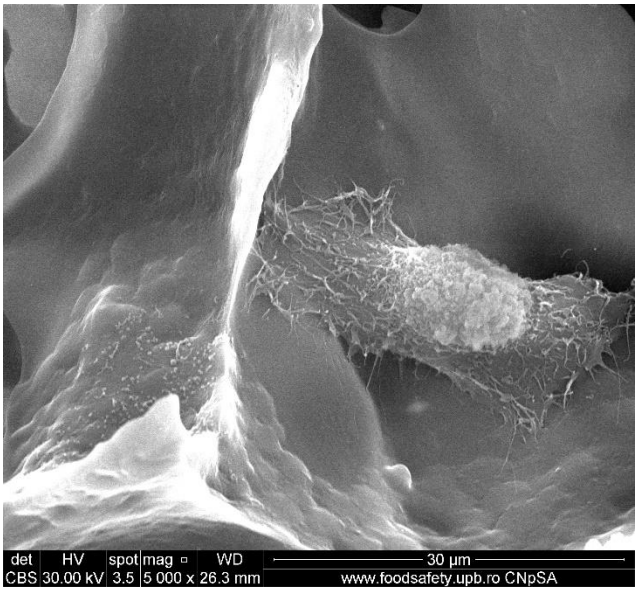

Fig.1.Osteoblast attached to the reference sample (gelatin-pectin crosslinked with GPTMS)

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Alginate-polyvinyl alcohol hybrid materials pH sensible

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An ideal drug delivery systems should protect the active substances by biological fluids attack, to transport them through biological barriers at the targeted sites in the right dose. Also it must be characterized by biodegradability and biocompatibility so that synthesized delivery system compounds to be harmless to the body. For oral administration the delivery system has to travel through stomach (low pH body fluid) without releasing the therapeutic agent. The drug release has to be triggered in high pH body fluids (pH 6.8-7.5) [1]. Clay minerals like kaolin, halloysite, talc, sepiolite, montmorillonite are used in pharmaceutical field due to their high specific area and adsorption capacity. In drug delivery field halloysite is intensively used because it presents a lumen where different types of active substances could be loaded and so the clay acts as a carrier.

In order to enhance the drug entrapment efficiency and improve the swelling behaviors of drug delivery system, Ca^{2+} crosslinking and freeze-thawing cycle techniques were used to prepare sodium alginate/polyvinyl alcohol hydrogel beads. Freezing–thawing process is the most facile method to produce physically crosslinked polyvinyl alcohol gel because it does not require the presence of crosslinking agent that may cause toxicity. The high porosity that is induced by freeze-thawing process will induce a severe burst release of an active ingredient. The presence of clays will act like a barrier and drastically reduce the burst release. In drug delivery field halloysite is intensively used because it presents a lumen where different types of active substances could be loaded and so the clay acts as a carrier[1]. The aim of this study is to obtain superporous hybrid beads of sodium alginate and halloysite using polyvinyl alcohol as a template. The alginate/ halloysite beads were prepared by electrospraying technique. Briefly in a alginate/polyvinyl alcohol were dispersed the active ingredient and different amounts of halloysite. The obtained suspensions were electrosprayed in a $CaCl_2$ solution The obtained beads were maintained for 2 h at freezing followed by 1 h of thawing. The freeze-thawing cycle was repeated 3 times and then the beads were intensively washed with water in order to remove the polyvinyl alcohol. In order to be characterized the obtained alginate/halloysite beads were freeze dried. The microparticle were characterized by FTIR, DCS, DLS, optic microscopy, *in vitro* drug release.

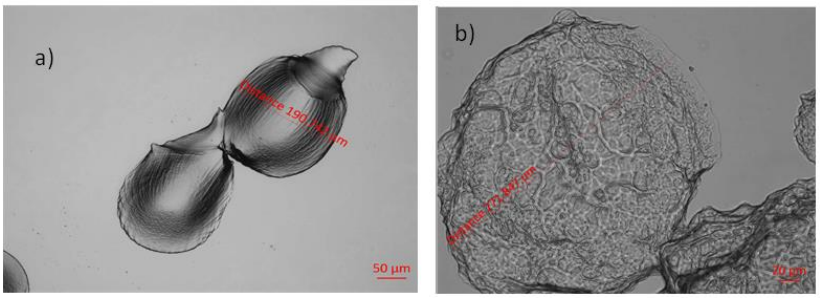

Fig. 1. Optical microscopy image: a) electrosprayed alginate/halloysite beads; b) freeze-thawed alginate/halloysite beads

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Electrospun fibrous architectures based on natural polymers-GO-COOH: design, formulation and in vitro characterization

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Rationally designed electrospun scaffolds based on natural polymers that, on the one side can mimic the structure and biological functions of extracellular matrix, and on the other can provide physical support for cells, are of particular interest to biomedicine.
The main objective of this study is to design, formulate and in vitro analize GO-COOH decorated bicomponent hybrid scaffolds with nanofibrous architecture as biomaterials with potential application in functional restoration of damaged tissue (Fig.1). Gelatin (Gel) and alginate (Alg), two natural polymers with high biocompatibility and microenvironment biomimicry along with carboxylated graphene oxide (GO-COOH) were rationally combined into the matrix of scaffolds, while the nanofibrous architecture was achieved through electrospinning method. The nanofibrous architecture of scaffolds along with the presence of GO-COOH on the surface of hybrid scaffolds were highlighted in SEM micrographs, while the occurence of different interactions between the functionalities of the system 'entities were observed in structural investigations (FTIR, Raman spectrometry). The in vitro biological assessments performed on fibroblast cells culture, indicated a good cytocompatibility and proliferation ability of bicomponent scaffolds with 0.1%wt. GO-COOH (MTT assay) along with a low cytotoxic potential (LDH test), suggesting their potency to support cells adhesion, growth and proliferation, as well as their potential use in tissue engineering.

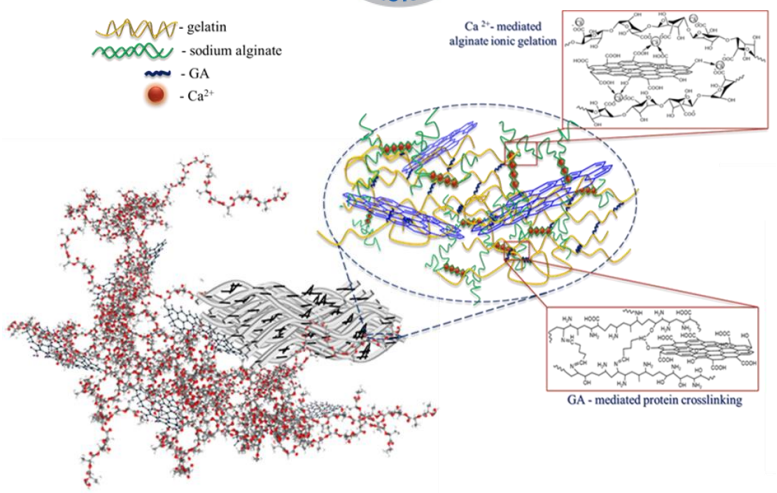

Fig.1 Schematic representation of the main concept in formulation of electrospun fibrous architectures based on natural polymers-GO-COOH

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Evaluation of novel biohybrid enriched with natural compounds for potential chemoprevention applications

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Introduction: Cutaneous melanoma is one of the most aggressive types of cancer, often fatal in metastatic stages, and current treatment options have limited efficiency. The term "chemoprevention" broadly refers to the use of pharmacological or natural agents to inhibit tumor initiation, promotion and progression. It has remained an area of active investigation since its inception. Among the natural agents being considered for chemoprevention are phytocompounds, such as curcumin (C) and quercetin (Q), with desirable anti-inflammatory, anti-oxidant and anti-tumor properties. However, the poor solubility and bioavailability of unmodified C and Q has limited their therapeutic applications. In this context, the aim of our research was to investigate the effect of novel microcapsules containing C or Q, embedded in a collagen-sericin (Coll-SS) scaffold, on cutaneous cancer cells, in order to determine their potential for future chemoprevention applications.

Experimental methods: Collagen-sericin tridimensional biomaterials enriched with curcumin or quercetin microcapsules (Coll-SS-C/Coll-SS-Q) were developed and characterized using scanning electron microscopy (SEM). Each composition was seeded with human primary melanoma cells and kept in standard culture condition for up to 7 days. To assess cell viability and proliferation, MTT assay was performed, after 3 and 7 days in culture, while determination of lactic dehydrogenase (LDH) content in the culture medium served as an indicator of the biohybrids' cytotoxicity. The ratio between live and dead cells was also determined using Live/Dead staining and confocal microscopy. Furthermore, cellular adhesion was investigated through immunostaining of actin microfilaments and visualization with laser-scanning confocal microscope.

Results and discussion: All samples exhibited a uniform porous structure with interconnected pores as shown by representative SEM images. Biocompatibility assessment performed after 3 and 7 days, respectively, revealed the effect of encapsulated C and Q on the viability, proliferation and cytoskeleton distribution of melanoma cells. Lower viability rates and decreased cell proliferation were observed on the Coll-SS materials enriched with either C or Q microcapsules after 7 days of *in vitro* culture, when compared to the simple control (Coll-SS) and the initial evaluation performed

after 3 days of culture in standard conditions. Moreover, cytoskeleton staining revealed the loss of proper adhesion to the Coll-SS-C and Coll-SS-Q substrates, highlighting a rounded tumor cell morphology, compared to the elongated actin microfilaments visualized on the Coll-SS control.

Conclusions: Our results emphasize the cytotoxic effects of curcumin and quercetin, suitably delivered through the use of embedded microcapsules, on skin cancer cells. Lower levels in terms of viability, proliferative capacity and cellular adhesion were registered on the scaffolds enriched with these natural compounds, with slightly better results obtained for Coll-SS-C. As such, these novel compositions present interest for further studies regarding their anti-tumor properties and potential chemoprevention applications.

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Oxidation of limonene to 1,2-Cyclohexanediol, 1-methyl-4-(1-methylethenyl) over carbon-supported titanium-benzoxazine complex catalyst

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Introduction: The use of renewable resources in the production of the chemicals was becoming more asking in the present context. Among these resources a significant attention has been attracted by limonene due to its relatively low cost, easy attainment from a renewable natural source and especially for its oxidation to high added value compounds [1]such as poly(limonene carbonates) [2].In light of above considerations, the aim of the present study was oxidation of limonene over carbon-supported Ti-benzoxazine complex catalysts.

Experimental: The carbon- supported Ti-benzoxazine complex (BZ) was obtained by the carbonization/activation of the coffe grounds. The synthesis of the titanium complex was carried out in chloroform and involved a molar ratio of titanium chloride /benzoxazine(3,3'-ethylene-bis(3,4-dihydro-1,3-benzoxazine) equal to 0.25: 1; 0.37:1 and 0.5:1. The materials prepared were characterized by ATR-FTIR and XPS. The oxidation of limonene to oxygenated compounds such 1,2-cyclohexanediol, 1-methyl-4-(1-methylethenyl) with H_2O_2 was carried out at 70 ºC for 6h in acetonitrile and reaction products were analysed by GC-MS and GC-FID techniques. The stability of catalyst was carried out for three catalytic cylces.

Results and Discussion: The presence of titanium on the surface of activated carbon was highlighted by the bands at 1642 and 749 cm^{-1} which can be assigned to Ti-OH and Ti-O-C bonds [3,4]. Moreover, XPS analysis also confirmed the presence of titanium on the surface of the carbon. The oxidation of limonene over carbon-supported Ti-benzoxazine complex led to an increase of limonene conversion to its oxygenated derivatives from 12% (for 0.06g Ti-BZ molar ratio 0.25:1) to 40% (for Ti-BZ molar ratio 0.37:1).

Conclusions: In summary, the present study described the catalytic performance of carbon-supported Ti-benzoxazine complex catalysts in the oxidation of limonene.

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Novel 3D Printed Polysaccharide/Clay Biomaterials

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Materials that are combined to form nanocomposites must contain at least one nanodimesional size partner. These compounds are anticipated to overcome the characteristics of the ingredients in a synergistic way and may combine various physical and chemical qualities. In this regard, combining hydrogels with inorganic nanofillers can significantly enhance their weak mechanical features. Three-dimensional polymer networks, called hydrogels, have a remarkable capacity to absorb water or biological fluids without dissolving. Hydrogels can be categorized as either synthetic or natural, as function of their source. The important characteristics of natural hydrogels are flexibility, biocompatibility, and availability of raw materials. Moreover, hydrogels can be used for a variety of purposes because of their structural similarity to the extracellular matrix. Chitosan, alginate, collagen, dextran, cellulose, hyaluronic acid, DNA, chitin, gelatin, and fibrin represent the majority of natural biopolymers used for hydrogels synthesis[1-3].
As previously indicated, incorporating nanoparticles into a hydrogel material is a viable way to get over the mechanical properties' restrictions. With the addition of nanoparticles, the subsequent physical and/or chemical interactions between nanofills and polymeric networks can produce nanocomposites with distinctive physically or covalently crosslinked architectures. Since the shape and structure of nanoparticles can vary, it is possible to use carbon nanotubes, ceramic, polymeric, and metallic nanoparticles, which can offer improved characteristics and tailored functionality[1-3].
This paper presents research studies regarding the printability and characterization of 3D nanocomposite hydrogels constructs based on natural polysaccharide with emphasis on the influence of Cloisites clay type on the printability and morphostructural properties.
The designed 3D printed nanocomposite structures are recommended as scaffolds with suitables properties for upcoming biological applications.

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Subprogram 1.2 -Institutional performance- Projects to finance excellence in RDI, Contract no. 15PFE/2021 and Nucleu Program 2023-2026, project code PN 23 26 01 01.

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Polypyrrole based thin films with ZnO for smart window applications

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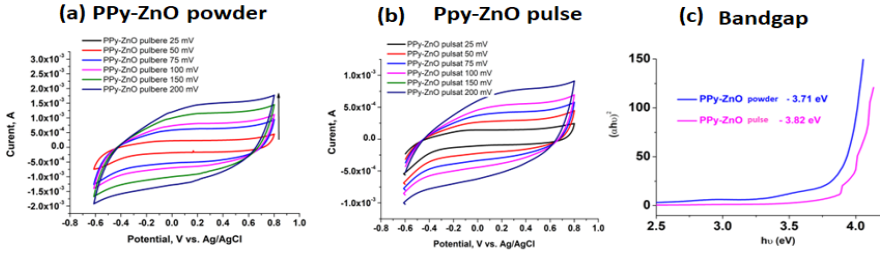
The aim of this research is to obtain stable ZnO-doped Polypyrrole (PPy) films on FTO substrate through electrochemical method. The doping of PPy with ZnO involves two processes: (i) *in first* an aqueous solution of pyrrole monomer with paratoluenesulfonic acid and 0.1 g ZnO powder, which was previously obtained from fibroin with $Zn(NO_3)_2 \cdot 6H_2O$ in ethanol (***PPy-ZnO powder*** film was obtained); and (ii) *in the second* the same aqueous solution of pyrrole monomer with paratoluenesulphonic acid, but with 0.05M $ZnNO_3$ precursor (***PPy-ZnO pulse*** film was obtained). The electrodeposition was carried out with an Autolab (PGSTAT 204) at 0.85 V applied and a load of 1 mC. The optical properties of two different coated films, ***PPy-ZnO powder*** and ***PPy-ZnO pulse,*** were evaluated and correlated with the electrochemical features. All the findings showed that the optimal electrical and optical properties of PPy-ZnO/FTO electrodes are obtained as a function of the ZnO doping method, making these electrodes suitable for developing new anode electrodes for smart windows applications.



(a) and (b) Cyclic voltammetry; (c) Band-gap values for PPy-ZnO powder and PPy-ZnO pulse films electrochemically deposited on FTO substrate.

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Graphene and Tamoxifen – a Molecular Dynamics investigation on potent anti-cancer complexes

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Around 70% of breast cancers are estrogen receptor-positive (**ER+**), with tamoxifen being most commonly used as an adjuvant treatment to prevent recurrence and metastasis. However, half of the patients will eventually develop tamoxifen resistance. Although new drugs are continuously being developed, in the case of cancer patients timing is crucial, and every new drug development comes with a specific high cost when it comes to time, especially atypical, novel molecules.

Graphene, although a novel material, has been already extensively studied due to being placed in the spotlight in hard working and cancer-relevant research communities as a consequence to its atypical and extraordinary properties. Although plenty of research is still underway, its about time to make use of the knowledge gathered thus far and taking quick steps towards practical, well-developed applications, for the benefit of society and fructification of the past years of research funding.

In the niche of cancer drugs, graphene qualifies both as a cancer-reducing drug and a drug delivery agent, making it an ideal platform for synergistic developments between the older, very well-known drugs, and novel improvements over current treatment protocols.

In the wet lab, graphene nanoribbons and tamoxifen have been investigated as a complex and have shown efficient cellular internalization and high target specificity for cancer cells, both in vitro cultured cells and mice. The two are hypothesized to complement each other beautifully, however they both bring challenges that have first to be addressed before moving forward: graphene is known to cause cell apoptosis, making it ideal if delivered on a very specific target, precisely the tumour. But the manner in which apoptosis takes place is hard to control, and may lead to fracturing a tumoral cell, allowing pieces of it to travel through the blood stream and present the risk of metastasis, releasing circulating tumour DNA. Taking into account that receiving too much graphene may do more harm to sensitive organs if overdosed due to its effective apoptosis inducing effect, it complements well with tamoxifen which can be used as an metastasis preventive agent, cleaning up the system of potential unwanted tumour pieces and thus reducing the aforementioned risks.

Designing an optimal therapy will still take some time, but it's even more promising than studies so far have shown given the multitude of derivatives graphene can be modeled into, through adding

functional groups on its surface, and the few forms of tamoxifen-alike molecules uncovered thus far, leading to a wide array of permutations for a truly beneficial and novel anti-cancer complex.

In this study we make use of atom-level in silico simulations, known as Molecular Dynamics, to investigate the interactions occurring between a tamoxifen molecule and graphene oxide in the presence of Mg^{2+} ions, opening up the wide array of potential permutations that can be investigated in atomic detail, as, to our knowledge – this specific application has not yet received attention for protocol development and force field optimizations.

We find that pi-pi interactions of the tamoxifen molecule are the main force behind its adsorption on graphene, which, in our case will preferentially take place nearby the oxygen-containing functional groups. Further on, we plan to investigate the amount of tamoxifen molecules that can be adsorbed on typical graphene oxide nano-sheets and the interactions between the novel complex and estrogen receptors.

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Hyaluronic Acid-Based Hydrogels as Potential Scaffolds for Tissue Engineering Applications

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Biocompatible and biodegradable hydrogels with biomimetic properties are increasingly interesting for biomedical applications, particularly when they can be printed or in situ formed to mimic extracellular matrix or as personalized implantable devices in tissue regeneration or drug delivery[1]. Hyaluronic acid (HA) is a linear anionic polysaccharide which is well known to be a primary component of the extracellular matrix which possess excellent moisturizing properties, biocompatibility and biodegradability, and also has a variety of essential physiological functions. Moreover, HA can bind to several receptors on the surface of cells and regulate cell activities, such as proliferation, survival, migration, and differentiation.

Among the many natural biomaterials found in the body, HA is a promising candidate for a broad range of biomedical applications such as fabrication of bioengineered scaffolds for cartilage, nerve, and skin tissues in addition to drug delivery systems. Notable concentrations of HA are present in synovial fluid, the vitreous body of the eye, cartilage, skin, the nervous system, and other tissues.

Apart from its numerous biological properties, HA also has a generous chemical structure that makes it an attractive biomaterial. The presence of a variety of functional groups such as carboxyl, hydroxyl and amide groups on HA backbone allow of ease of chemical modifications through which various mechanical and chemical properties can be tailored[2,3].

The aim of the present study was the chemical modification of hyaluronic acid with methacrylic anhydride in order to synthesize hydrogels with potential applicability in tissue engineering. The methacrylation reaction was confirmed through FTIR and 1HNMR. Hydrogel properties such as mechanical behavior, swelling as well as 3D bio printability were the main subjects of investigation.

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Rheological Investigation of Gelatin Methacryloyl /Guar Gum as a Potential Bioink

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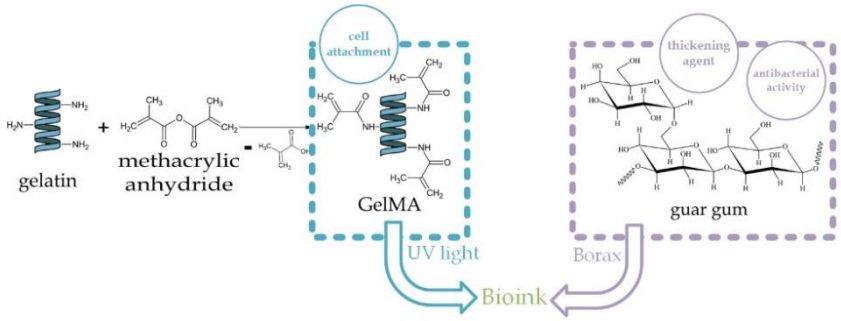
3D bioprinting is seen as a promising method for obtaining scaffolds for tissue engineering. In comparison, with other methods of fabrication of scaffolds, 3D bioprinting presents a major advantage regarding the capacity to adapt a very specific shape of each patient. More than that, 3D bioprinting allows the use of cell concomitant with the obtaining of the scaffold thus reducing the maturation time of the scaffold. The biomaterial or the combination of biomaterials which are used as bioink must be similar with extracellular matrix of the tissue, which is formed by a complex composition of fibrous protein and polysaccharide [1]. Gelatin is a fibrous protein, obtained by partial hydrolysis of collagen, which is present in its structure the tripeptide Arginine-Glycine-Aspartic Acid (RGD), a sequence that promotes cell attachment. At body temperature, gelatin is liquid which makes it unusable as a scaffold. Thus, in order to stabilize the scaffold is necessary to chemically modify gelatin in order to obtain photocrosslinkable gelatin which is known as Gelatin methacryloyl (GelMA). Unfortunately, GelMA presents low viscosity which leads to the collapse of the layers and limits its application as bioink. In order to improve viscosity, it was proposed to use a natural thickening agent: guar gum, a non-ionic polysaccharide. More than that, guar gum presents antibacterial activity [2]. Also, the use of a composition based on a protein and polysaccharide has the role to mimic natural extracellular matrix of the tissue.



Rheological properties of the bioink are very important. It is known that high viscosity ensures a good print fidelity, but high pressures are necessary to be used which may lead to cell damage. For extrusion based bioprinting, shear-thinning behavior is an essential factor governing printability, which means that with the increase of shear rate the viscosity decreases [3]. More than that, in order to have a good print fidelity it is important that after the shear stress is removed, the viscosity of the bioink to recover showing thixotropy behavior [4].

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Melt electrowritten scaffolds for bone surface reconstruction

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Osteonecrosis of the femoral head (FHON) is one of the depleting bone conditions characterized by the ischemic death of surface bone tissue in the femoral head, leading to significant impairment in terms of patients' quality of life [1]. As early-stage existing treatments and non-invasive approaches have limited efficacy, total hip arthroplasty remains the conventional solution for FHON [1]. Advancements in bone tissue engineering led to the fabrication of mechanically tunable scaffolds with precisely defined microarchitecture and cell-responsive behavior, aiming to facilitate patient-specific therapy and natural tissue regeneration [2]. This kind of structures should provide vascularization, mechanical structuring, multi-layering and control of geometrical factors [3].

The current landscape of additive manufacturing technologies has demonstrated exceptional versatility, enabling the construction of grafts and structures with diverse geometries to support tissue regeneration. Among these techniques, melt electrowriting (MEW), an integration of electrospinning and writing, has emerged as a highly promising approach for generating microfibrous elements with controlled geometries and porosity. By employing various 3D architectures, these scaffolds can serve as reinforcing elements for mechanically structured bone regeneration scaffolds (Figure 1).

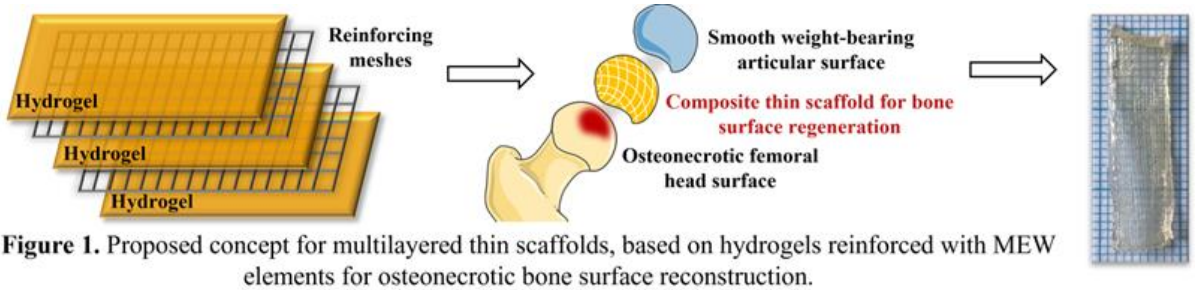

Figure 1. Proposed concept for multilayered thin scaffolds, based on hydrogels reinforced with MEW elements for osteonecrotic bone surface reconstruction.

We employed MEW to fabricate polycaprolactone (PCL) meshes that can be utilized to reinforce hydrogels. Our focus was on obtaining PCL elements based on 3D models with box sizes ranging from 250 to 1000 μm. We optimized the fabrication parameters to achieve filament and mesh shape fidelity. The effect of the geometrical parameters on the mechanical behavior is of major importance for the target application. Therefore, mechanical testing using a texture analyzer (traction tests) was performed, while the structural properties were analyzed by optical microscopy and microCT. The surface properties of the PCL elements were further modified via CO_2 plasma treatment for enhanced hydrophily and improved mesh-hydrogel interactions, while the efficiency of the surface

treatment was evaluated through contact angle. The developed PCL elements are promising as reinforcing agents for hydrogels, aiming to obtain hierarchically organized scaffolds for bone surface reconstruction.

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Optimization of Gelatin-PiPOx Precursors for Electrospinning Fabrication

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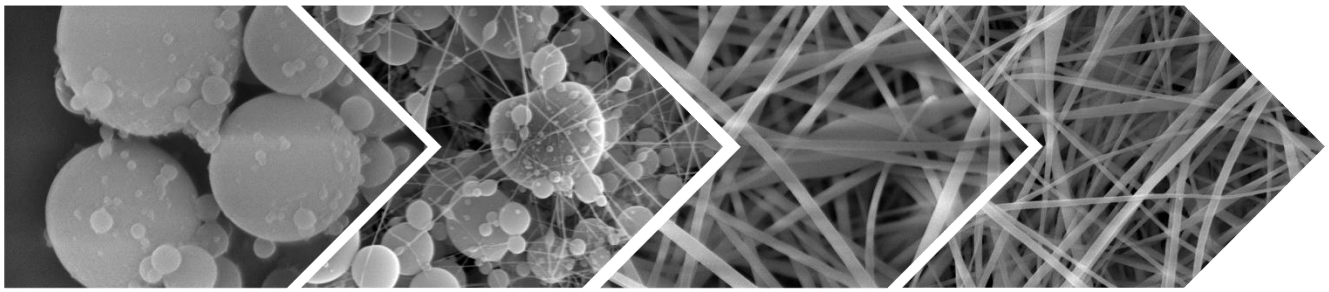
Introduction: The present work aimed at the development of hybrid fibrous scaffolds based on poly(2-isopropenyl-2-oxazoline) (PiPOx) and gelatin. PiPOx is a hydrophilic and biocompatible polymer that can be modified to introduce functional handles, by ring-opening addition reactions[1]. Fish gelatin (FG) is well known for its high biocompatibility and spinnability while its methacryloyl derivative (fGelMA) brings the possibility to crosslink the substrates through UV photopolymerization[2].

Methods: This study presents the optimization of the electrospinning fabrication of novel hybrid fibrous scaffolds based on FG or fGelMA and PiPOx. The FG-PiPOx and fGelMa-PiPOx fibrous substrates were fabricated using a controlled environment (25°C and 40% relative humidity) electrospinning equipment. Electrospinning precursors were prepared from aqueous solutions of the synthetic polymer and protein, in various ratios ranging from 1:10 to 10:1 w/w respectively. Morphological and structural characteristics were investigated through scanning electron microscopy and Fourier-transform infrared spectroscopy.
Results: This work reports on the optimization of electrospinning precursors for obtaining hybrid fibrous scaffolds with potential in biomedical applications. The presence of the synthetic polymer leads to beads formation within the obtained fibers. The best morphologies were obtained for fGelMA: PiPOx in a 10:1 wt/wt ratio.

Environmental parameters: 40% relative humidity, 25 °C



fGelMA: PiPOx 1: 10

fGelMA: PiPOx 10: 1

Figure 1. Representative morphological characteristics for fGelMA-PiPOx hybrid substrates

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Synthesis and evaluation of poly(propylene fumarate)-grafted graphene oxide as nanofiller for porous scaffolds

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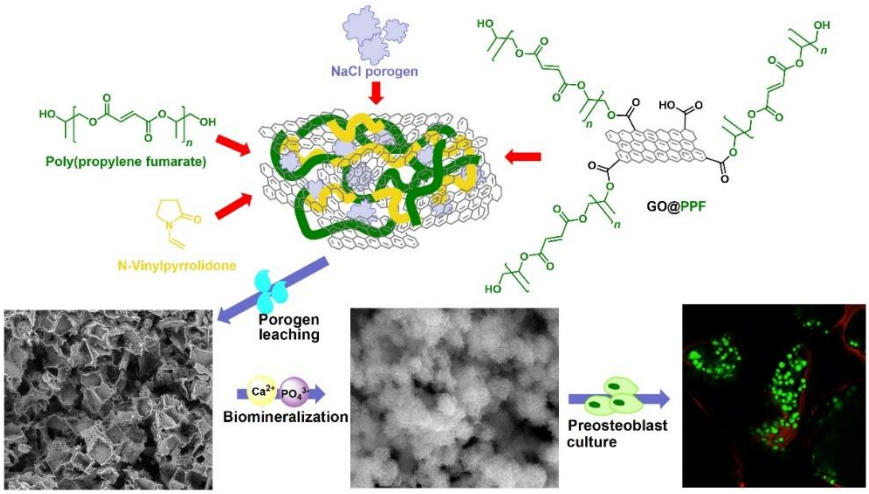
Recent advances in nanotechnology and polymer chemistry enabled the development of many advanced scaffolds for tissue engineering and regenerative medicine. Therefore, a variety of materials including hydrogels, porous nanocomposites and nanofibers have been investigated as potential candidates for bone repair [1]. Several aspects should be considered when designing scaffolds for tissue engineering applications, including mechanical properties, biodegradation rate, and biocompatibility in order to allow cell adhesion, differentiation and proliferation [2]. In an effort to obtain porous scaffolds with improved mechanical properties and biocompatibility, the current study discusses nanocomposite materials based on poly(propylene fumarate)/N-vinyl pyrrolidone (PPF/NVP) networks reinforced with polymer-modified graphene oxide (GO@PPF). The GO@PPF nanofiller was synthesized through a facile and convenient surface esterification reaction, and the successfull functionalization was demonstrated by complementary techniques such as FT-IR, XPS, TGA and TEM. The PPF/NVP/GO@PPF porous scaffolds obtained using NaCl as porogen were further characterized in terms of morphology, mechanical properties, sol fraction, and in vitro degradability. SEM and nanoCT examinations of NaCl-leached samples revealed networks of interconnected pores, fairly uniform in size and shape. We show that the incorporation of GO@PPF in the polymer matrix leads to a significant enhancement in mechanical properties, which we attribute to the formation of denser and more homogenous networks, as suggested by a decreased sol fraction for the scaffolds containing a higher amount of GO@PPF. Moreover, the surface of mineralized PPF/NVP/GO@PPG scaffolds is uniformly covered in hydroxyapatite-like crystals having a morphology and Ca/P ratio similar to bone tissue. Furthermore, the preliminary biocompatibility assessment revealed a good interaction between PPF/PVP/GO@PPF scaffolds and murine pre-osteoblasts in terms of cell viability and proliferation.



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Preparation and characterization of modified chitosan microparticles intended for controlled drug delivery

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The development of new delivery systems for the controlled release of drugs is one of the most interesting fields of research in pharmaceutical sciences. Microparticles can be used for the controlled release of drugs, vaccines, antibiotics, and hormones.[1] Natural polymers fulfil the stringent requirements of these drug delivery systems such as degradation within an acceptable period of time, controllable release of the drug and targeting of specific sites thus achieving a greater pharmacological response.[2]
In this study modified chitosan with methacrylated vanillin microparticles were obtained. Chitosan, a natural-based polymer obtained by deacetylation of chitin, is nontoxic, biocompatible, and biodegradable[3] which makes it a good candidate for novel drug delivery systems. In addition, mild interaction with cells, the mucosal membrane or tissue, which improves absorption or efficacy, is a property of chitosan microparticles. Vanillin is a natural monomer, used as a bio-based cross-linker for ultraviolet (UV)-induced bonding and Schiff-base bonding[4].
In the first part of this study, the methacrylation of vanillin was verified by both Fourier-transform infrared spectroscopy (FT-IR) and Nuclear magnetic resonance (NMR) spectroscopy. The second part is focusing on the chitosan modification with methacrylated vanillin through a Schiff base reaction forming the vanillin-chitosan derivative. FT-IR and X-ray photoelectron spectroscopy (XPS) as well as rheological study confirmed the grafting on chitosan chains. Finally the microparticles were obtained by emulsion polymerization (W/O) through UV light using Irgacure 2959 as initiator.

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Nafcillin-loaded nanocomposite hydrogels based on Poly(N-vinylpyrrolidone) for biomedical applications

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The present study describes the synthesis and the characterization of six novel nafcillin-loaded photopolymerized Poly(N-vinylpyrrolidone) based nanocomposite hydrogels. These innovative formulations demonstrate their performances as drug carriers and antimicrobial efficacy against gram-positive bacteria. The different nanocomposites were obtained based on amidic N-vinyl-2-pyrrolidone monomer and tri(ethylene glycol) divinyl ether crosslinker in an aqueous suspension of exfoliated hydrophilic bentonite nanoclay and/or two types of photoactive (TiO2 and ZnO) nanofillers, by using 2-hydroxy-4′-(2-hydroxyethoxy)-2-methylpropiophenone as a photoinitiator. Further, the hydrogels were evaluated through various analytic tools, such as Transmission electron microscopy (TEM), scanning electron microscopy - energy dispersive X-ray analysis (SEM-EDX), mechanical test (tension, compression, shear), ultraviolet-visible spectroscopy (UV-Vis), swelling investigations and via specific microbiology assays ('Agar disk-diffusion method' and the 'Time-kill test'). The results revealed that all nanocomposite hydrogel samples possess excellent mechanical resistance and good swelling abilities. The incorporation of nafcillin antibiotic remarkably contributed to the improvement of the antimicrobial activity of samples, demonstrating a decrease of bacteria growth between 3log10 and 2log10 after one hour of direct contact with S. aureus. American Society for Testing Materials – ASTM. (2009). ASTM D1434-82: Standard test method for determining gas permeability characteristics of plastic film and sheeting. Philadelphia: ASTM.

Collagen and Collagen-Keratin Nanofibers from Donkey Skin for Potential Medical Dressings

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Traditional wound care includes primary materials such as cotton gauze dressings, hydrogels, foams, composite dressings, non-adherent dressings, nets, impregnated gauze, natural materials such as leaves, and honey[1]. An ideal material used for the manufacture of medical dressings should possess a porous structure to absorb exudates over a period of time, be biocompatible, biodegradable, and safe, have mechanical properties similar to human skin, exhibit antimicrobial activities and antioxidants, promote cell adhesion to protect the wound from external factors such as desiccation and mechanical injury, and be cost-effective[2].

Donkey skin *(Equus asinus* L.) has long been used as a raw material for the preparation of gelatin (Colla corii asini), which is utilized as a food for treating anemia in traditional Chinese medicine for over 2000 years. Gelatin extracted from donkey hide shows promise as a bioresource for developing potential drugs and value-added products due to its abundant availability and biologically active properties. This study focuses on obtaining collagen nanofibers from donkey skin and collagen-keratin from donkey skin and hair using the electrospinning process with a collagen solution. The flow rate of the solution was set at 0.8 mL/h, the voltage at +22.71 kV, and the distance between the needle tip and collector at 14 cm.

Table 1 represents the physicochemical properties of collagen and collagen-keratin extracted from donkey skin.

Table 1. Textural characteristics and viscosity of collagen and collagen-keratin extracted from donkey skin and hair

Characteristics	Collagen from donkey skin	Collagen-keratin from donkey skin and hair
Dry substance, %	11.80	13.00
pH (1:10), pH units	7.2	9.10
Strength, g	321.00	421.00
Relax, %	21.50	17.40
Viscosity, CP	15.35	20.5
Electrical conductivity, mS/cm	10.84	9.04

The resulting nanofibers show potential application in obtaining of non-active medical dressings for wound healing.

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Polymeric Nano/Microcapsules Loaded with Dexamethasone for the Treatment of Pneumonia

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Pneumonia is an inflammatory condition of the lungs caused by infection with viruses, bacteria, parasites or fungi. Conventional treatment against bacterial lung infections is effective, but must be administered as combination therapy in high doses of drugs for long periods of time to maintain an optimal therapeutic level [1,2]. In this context, the aim of this study was to prepare and to characterize nano/microcapsules based on carboxylated chitosan and poly (vinyl alcohol) and loaded with Dexamethasone with potential applications in the treatment of pneumonia. The nano/microcapsules were prepared by the double emulsion–condensation method using [4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride] (DMT-MM) as an activating agent. The physicochemical properties of the obtained nano/microcapsules were assessed by different techniques, such as: DLS, SEM, FT-IR, UV-Vis. In addition, *in vitro* Dexamethasone release, biodegradability and hemocompatibility of the nano/microcapsules were also investigated.
Scanning electron microscopy (SEM), shown in Figure 1 showed that the synthesized nano/microcapsules are spherical, have a slight tendency to agglomerate, and show a high polydispersity, a fact confirmed by the DLS results.

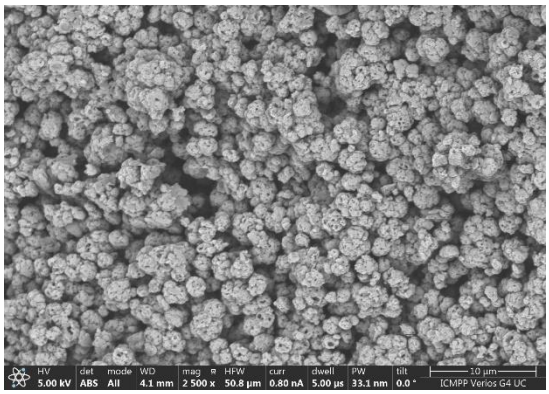

Figure 1. SEM microscopy for nano/microcapsules

The zeta potential was determined to investigate the stability of the capsules in the aqueous medium and was measured in a solution with pH = 7.4 to simulate physiological conditions. The zeta potential values varied between -17 mV and -25 mV. It was found that with the increase in the amount of PVA in the system, the values of the zeta potential decreased. The swelling degree of the

nano/microcapsules was investigated in phosphate buffer solution (pH = 7.4) and was imposed as a result of their potential use as drug carriers. The swelling degree of the obtained nano/microcapsules was strongly influenced by the initial ratio between the polymers. As the amount of carboxylated chitosan in the system increased, the swelling degree increased. The release efficiency of Dexamethasone from the nano/microcapsules was between 80% and 90%. All the obtained samples were biodegradable and hemocompatible.

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Nanostructured double-network systems of polyacrylamide and mucin-functionalized nanodiamonds

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Introduction: Polyacrylamide hydrogels are vastly used for various biomedical applications due to their ability to absorb large amounts of water. However, these materials have relatively weak mechanical properties and are biologically inert. To improve these aspects, several routes have been studied, including nanostructuring and the addition of natural cell-friendly polymers. The present work proposes a simple route for the synthesis of a double-network nanostructured material with improved mechanical performances. Using the described procedure, the double network materials are generated through the incubation in a polyphenol solution of PAAm hydrogels nanostructured with mucin-functionalized nanodiamonds.

Method: Firstly, porcine gastric mucin (PGM) was adsorbed on diamond nanoparticles (NDs), resulting in a PGM-functionalized NDs (PGM@ND). Then, the monomer - acrylamide (AAm), crosslinker - methylenbisacrylamide (MBA), and initiator system were added. The system was also supplemented with linear PAAm, as viscosity modulator [1]. The precursors were poured in molds and the polymerization was allowed for 2 hours at room temperature. After purification with distilled water, samples were immersed in tannic acid (TA) bath with different concentrations.

Characterization: PGM's adsorption on NDs was confirmed through FTIR, the registered spectra showing that the functionalized nanoparticles present the characteristic vibrations of the glycoprotein. The DLS measurements also confirmed the success of the adsorption, indicating that a series of interactions (hydrogen-bonding) occurred, modifying their diffusion coefficient, hydrodynamic features, and stability. Furthermore, the rheologic measurements performed on the precursors confirmed the improved stability of the PGM@ND dispersion when compared to the ND dispersion and PGM solution. The addition of the linear PAAm in the precursor further improves the stability of the polymerization compositions.

The investigations performed on the double-network hydrogels revealed that the concentration of the TA bath has a significant influence on the mechanical properties of the materials, both at macro and micro-scale. The rheologic tests indicated that increasing the concentration of polyphenol leads to materials with a lower elastic modulus (G') and a higher viscous modulus (G"), suggesting that the generation of a denser secondary network leads to materials that are less stiff and have greater ability to dissipate energy upon stress. Furthermore, the nanoindentation tests revealed that both G' and G" increase with increasing TA concentration. As the generation of the secondary network was performed through incubation in a polyphenol solution, it is expected that the second-network systems present a shell-like surface.

Conclusions: This study demonstrates that a high mass glycoprotein can be adsorbed on the surface of carbon-based nanospecies through a simple procedure. The functionalized particles were used as

nanostructuring elements in a polymeric network and the functional groups of the so-adsorbed macromolecule represented sites for the generation of a secondary H-bond network. The resulting materials are less stiff and display an improved ability to dissipate energy under stress, being good candidates for various biomedical applications.

Acknowledgments: This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS-UEFISCDI, project number PN-III-P1-1.1-TE-2019-1161, within PNCDI III. The nanoindentation measurements were possible due to the project INOVABIOMED P_36_611 (MySMIS code 107066).

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Fibrous biomaterials with antibacterial activity and potential applications in dermal treatments

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Introduction: Fibrous biomaterials with antibacterial properties have evolved as useful instruments for cutaneous treatments. In addition to promoting wound healing and treating skin infections, these biomaterials also prevent bacterial development. Their uses range from burn treatment to skin care products for acne and dermatitis to the treatment of chronic wounds and wound dressings [1,2]. These designs contain the potential for further developments in the industry and provide promising solutions for cutaneous health. Thus, the main goal of this study is to formulate a biodegradable electrospun biomaterial with antibacterial activity as potential candidate used in the dermal treatment.

Experimental methods: Gelatin in a concentration of 40wt.% was used to formulate the electrospun matrix, while two different concentrations of the antibacterial agent tetracycline hydrochloride (TCH) were selected to be loaded within the electrospun fibers, in order to formulate the biodegradable electrospun biomaterial with antibacterial activity. The detailed composition of the formulated biomaterials was presented in Table 1.

Table1. The composition of the samples

Sample	Volume (mL)	c Gelatin (%)	Wt. Gelatin (g)	Wt % TCH	Wt. TCH (g)
Gel	5	40	2	-	-
Gel-TCH 1%	5	40	2	1.0	0.02
Gel-TCH 2.5%	5	40	2	2.5	0.05

The solutions were homogenized under stirring at 37°C and the complete homogenized precursor solutions were subjected to electrospinning process using a climate-controlled electrospinning equipment (IME Technologies, Netherlands), selecting the technical parameters that generated continuous and uniform fibers. The formulated fibrous biomaterials (Gel, Gel-TCH 1%, and Gel-TCH 2.5%) were cross-linked using glutaraldehyde vapor for approximately 4 hours to enhance stability, following their washing with water to remove residual glutaraldehyde and other chemicals and then dried in an oven.

Results and discussion: The obtained biomaterials were investigated through different techniques: structural characterization (FTIR) revealed the chemical composition of biomaterials and the potential interactions between the Gel matrix and therapeutic TCH; morphological analysis (SEM)

showed the uniformed and continuous fibrous architecture of biomaterials. Swelling and degradation experiments of scaffolds suggested that both the presence of collagenase and the TCH loading impacted the stability of scaffolds in biological environments, while the TCH release profile is highly dependent on the enzyme presence. Moreover, the biological investigations (MTT, LDH and Live/Dead tests) suggested a good biocompatibility of scaffolds along with some cytotoxic response in the case of Gel-TCH 2.5%, attributed to an increased concentration of antibacterial agent TCH.

Conclusion: Fibrous biomaterials based on gelatin and loaded with tetracycline were formulated and investigated as potential antibacterial candidates used in skin treatment. According to structural, morphological, biological and stability studies the obtained biomaterials showed advantageous structural characteristics, regulated tetracycline release, and acceptable biocompatibility, demonstrating their potential for application in dermal treatment.

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Functionalized graphene oxide with antibacterial properties for photothermal therapy

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Photothermal therapy has recently become a promising strategy in healing wound infections caused by bacteria colonization that tend to develop resistance against antibiotic treatments [1]. Graphene oxide (GO) is a promising candidate that can act against bacterial infections being used as a photothermal agent due to its ability to absorb near-infrared (NIR) light energy, inducing a local hyperthermia that will permanently destroy bacteria [2]. However, GO does not exhibit ideal antibacterial activity due to its tendency to agglomerate under biological conditions, but also due to its negatively charged surface, which limits its interaction with bacterial cells [3],[4].

In this study, to improve the antibacterial properties, initially the GO surface was functionalized with branched polyethyleneimine (BPEI), using an EDC (N, N-(3-dimethylaminopropyl)-N-ethyl carbodiimide/NHS (N-hydroxysuccinimide) coupling system. The chemical modification of GO with BPEI led to the formation of amide bonds between the carboxyl groups (-COOH) and the epoxy groups of GO and the amino groups ($-NH_2$) of BPEI. The functionalization of the GO surface with BPEI was confirmed by using Fourier-Transform Infrared Spectroscopy (FTIR), Raman Spectroscopy, X-Ray Photoelectron Spectroscopy (XPS) and Thermogravimetric Analysis (TGA).

The functionalized GO can be further involved in a Schiff base reaction by forming an imine bond between an amino group on the functionalized GO surface and an aldehyde group, which will lead to the development of a hydrogel in which the dispersibility of GO will be improved, as well as the antibacterial activity. To obtain aldehyde groups, the hydroxyl groups (-OH) on the sodium alginate backbone were involved in an oxidation reaction in the presence of an oxidizing agent, namely sodium periodate ($NaIO_4$) [5]. Oxidized alginate was characterized by Fourier-Transform Infrared Spectroscopy (FTIR) and Proton Nuclear Magnetic Resonance (^{1}H NMR), and in addition the content of aldehyde groups was determined by hydroxylamine hydrochloride titration. Furthermore, the functionalized graphene oxide-based hydrogel can be used in combination with photothermal therapy to eliminate bacteria that adhere to the surface of skin wounds.

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Nanoparticles based on Functionalized Albumin Cross-linked with Oxidized Polysaccharides Used for Drug Delivery in Brain Tumors Therapy

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This work aims to develop a new drug delivery nanosystem based on human serum albumin (HSA) functionalized with low molecular weight protamine (LMWP), cross-linked with aldehyde groups from oxidized gellan or oxidized pectin, containing two antitumor drugs (curcumin and temozolomide) co-encapsulated, able to overcome blood-brain barrier (BBB) which is a considerable obstacle in drug delivery and to treat brain tumors.
In the first step, HSA was modified with LMWP, a peptide used to improve the diffusion coefficient of albumin to the brain. Drug delivery into brain cancer tumors can be enhanced by targeting strategy mediated by HSA and BBB overcoming, mediated by LMWP[1]. Salmon protamine sulfate was proteolytically cleaved in the presence of thermolysin in order to obtain LMWP. FT-IR and NMR spectroscopy results confirmed that HSA could be functionalized with LMWP at the free SH group from Cys34 residue.
An improved HSA self-assembly method was used to obtain the nanoparticles. When β-mercaptoethanol is added to the HSA solution, the disulfide bonds are reduced at SH groups. Thus the hydrophobic domains are exposed to interact with the hydrophobic drugs and will finally self-assemble into nanoparticles[2]. In order to increase the nanoparticle stability, the cross-linking of free NH_2 groups from HSA with aldehyde groups from oxidized polysaccharides was performed. $NaIO_4$ was used to oxidize the polysaccharides, and the presence of aldehyde groups was demonstrated by FT-IR and NMR spectroscopy. The morphology of the nanoparticles was analyzed by scanning electron microscopy, and their size determined by laser diffractometry was up to 200 nm. FT-IR spectroscopy demonstrates the Schiff base formation. The curcumin immobilization efficiency was higher than the one of temozolomide and decreased when the cross-linking degree increased. Temozolomide can form polymer-drug conjugates through the interaction of amine groups within its structure with free aldehyde groups within oxidized polysaccharides. The *in vitro* release kinetics was studied in two different pH environments at pH=7.4 and pH=4. The HSA-based nanoparticles having temozolomide and curcumin immobilized determine the drug protection, increase

bioavailability, eliminate side effects, and ensure a controlled and sustained release at therapeutic doses.

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Graphene oxide/Nitrocellulose non-covalent hybrid as solid phase for oligoDNA extraction from complex medium

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Commercially nitrocellulose (NC) membrane non-covalently modified with graphene oxide (GO) microparticles were successfully prepared for oligonucleotide extraction. The GO was utilized due to the high adsorption of bio-receptors on its structure, and also supports the detection of cells, molecules, ions, and nucleic acids by promoting a quenching effect on them.

Our work manipulated the low affinity of double-stranded DNA to the GO site, exploiting this as a "turn-off" trial to identify the quenching base hybridization of a single-stranded (ss) DNA probe. Membrane surface properties such as hydrophilicity, pore size, charge density, and roughness are important properties involved in membrane separation performance and antifouling characteristics. Modification of membrane surface properties could significantly improve the efficiency of the membranes. This type of membrane with minimal modification to the membrane's intrinsic structures represents good potential for implementing such an approach on commercially available nitrocellulose membranes. Thus, the GO-modified NC membranes were applied to separate the oligo DNA (<50 nt) from a complex solution. The oligonucleotides were readily adsorbed to and readily desorbed from the surface of the GO-modified nitrocellulose membrane by Tris-HCl buffer pH 8.0. We resorted to using different DNA adsorption times more specific 30, 45 and 60 min and a desorption time of 45 min to quantify the results difference.

By using a fluorophore-labeled aptamer the fluorescence assay demonstrates that the GO-NC hybrid offers better DNA adsorption to the membrane surface than the control utilized. The amount of oligo DNA extracted by the GO-modified NC membranes was 330-370 pg (~7%) from the started total amount. These results demonstrate that the method of short oligo DNA separation by using GO-modified NC membranes as a solid phase adsorbent is an efficient and simple way to purify short oligonucleotides from complex solutions. Thus, we propose the use of nitrocellulose-graphene oxide solid phase as an alternative/complementary procedure to the commercially magnetic beads extraction kits.

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Composite injectable hydrogels based on chitosan and graphene oxide with applications in photothermal therapy

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Hydrogels exhibit a lot of applications in the biomedical field, such as scaffolds for tissue engineering, in bioprinting, as carriers in controlled drug delivery systems or in the fabrication of biosensors [1]. Properties such as biocompatibility, biodegradability, easily tunable mechanical and rheological properties and their biomimicry of natural extracellular matrix make hydrogels an attractive choice of materials to be used in biomedical applications [2]. Moreover, injectable hydrogels present additional advantages in the form of having a minimally invasive administration, with reduced infection rates in comparison with implanted materials and decreased procedure costs. The basic principle of photothermal therapy relies on the ability of certain materials (called photothermal agents, PTA) to absorb and to convert electromagnetic energy to thermal energy [3]. In the specific case of hydrogel-based photothermal therapy systems, the hydrogel represents a matrix which incorporates PTAs that will generate heat under the effect of near infrared (NIR) light. This heat will diffuse throughout the hydrogel and spread to the surrounding tissues, causing local overheating and then thermal ablation of tumor cells (in the case of cancer eradication applications). In terms of possible materials that can be used to obtain these injectable hydrogels, polysaccharides are one of the most used class of materials. Chitosan (CS) is one of such polysaccharides, that has been extensively studied with regards to biomedical applications of hydrogels. The main limitation of CS is represented by its poor mechanical properties. One of the most common approaches that can be adopted to improve mechanical properties is the incorporation of carbon-based materials, such as graphene oxide (GO).

A gelling system for the development of chitosan hydrogels that has been researched less is the gelation of chitosan using sodium bicarbonate. The principle behind this system is based on the neutralization of CS by carbonic acid (resulted from the decomposition of sodium bicarbonate). This reaction, along with the increase of temperature, decreases the electrostatic repulsion between CS chains and allows for the formation of a three-dimensional CS network. Furthermore, the production of carbon dioxide (CO_2) causes an increase in the solution's pH and leads to gel formation.

In this work, an injectable hydrogel based on CS and modified GO (GO-COOH) was successfully synthesized. The necessary basic conditions for this material were met, meaning its injectable character, by easy extrusion through the needle of a syringe, and its thermo-responsive character, by gelling exclusively at temperatures higher than 37°C. By characterizing the material, it was

confirmed that interactions between chitosan and graphene indeed formed, this being verified both by Fourier transform infrared spectrometry (FTIR) and by thermogravimetric analysis (TGA). The material exhibits a high equilibrium swelling degree, with a high-water absorption capacity, it is biodegradable, and has a superior thermostability compared to the individual component materials. This hydrogel presents potential application in PTT and, subsequently, in cancer treatment or wound healing therapies. Finally, with the incorporation of an antitumor drug, a synergistic effect could be achieved by chemo-photothermal therapy.

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Hyperbranched PEI-PEG/DNA Polyplex Formation: a Molecular Dynamics Study

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PEGylated PEI's are among the most studied non-viral vectors for gene delivery, having one of the highest transfection efficiency. We analyze the interaction of hyperbranched polyethylenimine polyethylene glycol (HPEI-PEG) with DNA, for different number of PEG chains per HPEI core, by all-atom molecular dynamics simulations. To this end, a new CHARMM Force Field for PEG was developed. The obtained parameters for bonds, angles, and dihedrals are validated by the good agreement with experiment, in terms of radius of gyration and diffusion coefficient. For adjacent PEG and PEI monomers, the parameters were adjusted to fit quantum mechanical target data by imposing that the partial atomic charges remain unchanged from the already optimized PEG and PEI monomers.

For the DNA-polycation simulations, to a protonated HPEI core of 3.12 kDa molecular weight, up to 6 PEG chains were attached, while varying the PEG molecular weight between 0 and 4.94 kDa. The DNA model was obtained by essentially concatenating three Drew-Dickerson dodecamers. The solvated systems were neutralized by adding an adequate number of Na counterions. In order to not favor the DNA-polycation complexation, the initial configuration was chosen with the copolymer placed perpendicular to DNA, at 50 Å distance from its center of mass.

Mainly due to the electrostatic interaction between the protonated amines in PEI and negatively charged phosphate groups in the DNA's backbone, the polycation diffuses towards DNA. The equilibrium distribution of the protonated PEI nitrogens around the phosphorus atoms in the DNA backbone shows a sharp peak around 4 Å, indicating that hydrogen bonds are formed. This occurs regardless of the PEG density, implying that DNA condensation does not depend on PEG/PEI ratio in the range studied here.

The PEG's role appears to improve solubility, which is seen by the increased number of water molecules in close proximity to PEG in comparison to PEI. Moreover, PEG masks the surface charge of the polyplex, as demonstrated by the distribution of PEG chains around phosphorus atoms in the DNA's backbone, reducing the compounds cytotoxicity. In comparison to PEI's distribution around DNA, PEG's distribution is broader indicating that PEG chains are free to move around DNA.

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NIR-797 Loaded Poly (Lactic-co-Glycolic Acid) Nanoparticles as Phototherapeutic and Fluorescent Contrast Agents

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Fluorescent nanoparticles provide excellent applicability within cancer-related diagnostics by account of their ability to provide real-time distinction between malignant cells and healthy tissue for image-guided surgery. In contrast to traditional clinical imaging, fluorescence-based imaging techniques offer more rapid and sensitive results, allowing us to explore many cellular processes instantaneously. Because of the autofluorescence and attenuation in the visible light spectral region of the biological matter (400 – 650 nm), for the deep tissue imaging applications have been developed fluorescent nano-sized agents in the Near-Infrared (NIR) spectral region (650 – 950 nm)[1].

The polymer poly (lactic-co-glycolic acid) (PLGA) is being used in many long-acting drug formulations for drug delivery in cancer, being approved by the Food and Drugs Administration (FDA) and promoted for its high biocompatibility and safe biodegradability[2]. In light of the aforementioned aspects, the present study investigates the benefits of pre-clinical implementation of PLGA nanoparticles, using an emulsion method to load a NIR fluorophore, i.e., NIR-797-isothiocyanate (PLGA@NIR797 NPs). Specifically, a first indicator regarding the good stability of the newly fabricated PLGA@NIR797 NPs was provided by Zeta-potential measurements (-55.0 ± 1.0 mV) and Dynamic Light Scattering (DLS) measurements which show an average hydrodynamic diameter of 238 ± 4 nm, with a PDI of 0.19 ± 0.01, size that was also confirmed by transmission electron microscopy (TEM) imaging. The successful encapsulation of the NIR-797-isothiocyanate dye was confirmed by the recorded emission maximum of PLGA@NIR797 NPs at 808 nm, with a loading efficiency of 89.0 ± 0.4 %. The biodegradability of the synthesized nanoparticles was also studied and confirmed by DLS measurements, fluorescence intensity and absorption spectra. More importantly, the ability of the PLGA@NIR797 NPs to operate as effective phototherapeutic agents in solution by generating heat under NIR laser irradiation (i.e., 808 nm laser) was then evaluated, showing a rise in temperature of 9ºC in 4 minutes. Finally, the viability - proved by MTT assay - and *in vitro* cellular uptake - confirmed by confocal fluorescence imaging - of the free NIR-797-isothiocyanate and PLGA@NIR797 NPs were assessed in melanoma cells (i.e., B16 - F10 cell line).

To summarize, this study presents the effectiveness of the PLGA@NIR797 NPs as innovative NIR contrast agents for fluorescence imaging due to their good loading efficiency, time and size stability, as well as their biocompatibility, biodegradability and photothermal capability.

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On How Graphene Oxide Ratio Impacts Mechanics-Architecture-Fluidity in Double-Reinforced Fish Gelatin Composite Scaffolds

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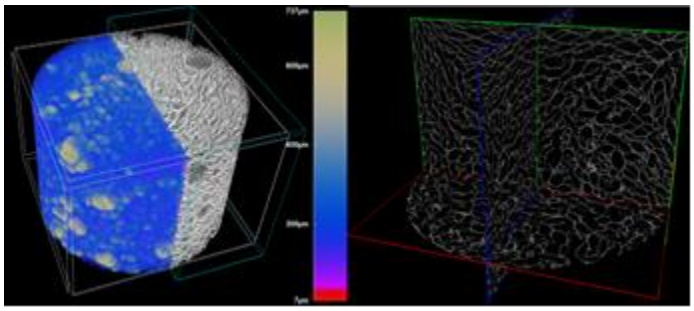
The preparation of genipin crosslinked composite blends of fish gelatin and kappa-carrageenan (fG/κC) with varying percentages of graphene oxide (GO) for use as osteochondral substitutes was accomplished through the use of a straightforward solution-blending technique. In this research, we emphasized a causality between the morphology/in vitro stability behavior and the stiffness of fG/κC hydrogels that were reinforced with exponentially variable GO fractions. The reorganization of the network that was caused by the GO had an effect on the composite gel's elasticity, and we believe that this effect further controlled the pore patterning and solid phase structuration. Micro-computer tomography, swelling investigations, enzymatic degradations, compressions tests, MTT, LDH, and LIVE/DEAD assays were all used to investigate the structures that resulted. The data that were derived showed that genipin crosslinked fG/κC blends that were reinforced with GO have a homogeneous morphology with optimal pore diameters of between 200 and 500 μm for use as a substitute in bone tissue repair. The fluid absorption of the blends was improved by the addition of GO at a concentration greater than 1.25 wt. %. After ten days, the blends will have degraded completely, and the gel fraction stability will have increased in proportion to the amount of GO present. First, the blend compression modules started to decrease until a minimum low for fG/κC_GO3 sample. After that, upon increasing the GO concentration, the blends to start regaining their elasticity. With an increase in GO ratio, the MC3T3-E1 cell viability assay showed a decrease in the number of viable cells however, the LDH and the LIVE/DEAD assays were within the acceptable standardized limits in terms of healthy and live cells in all of the composite blends. By comparing GO concentrations, we were able to discover non-linear fluctuations in the mechanical properties of these hydrogels. These fluctuations generated a ripple effect in the geometry and in vitro behavior of the hydrogels. In addition, on the basis of these data, future research could concentrate on narrower, more personalized amounts of GO reinforcement in order to achieve more precise results.



3D morphological analysis of the solid phase architecture and porosity in fGκC composition

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Functionalization of Polysulfone Membranes with Cyclodextrin based-Supramolecular Architectures

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The development of novel polymeric composites membranes for hemodialysis represents a compelling and demanding research topic in membranes engineering. Generally, the hemodialysis membranes are obtained from cellulose acetate, polysulfone (PSF) and polyethersulfone (PES) [1, 2]. Polysulfone is widely used in the production of hemodialysis membrane due to its remarkable properties, such as good solubility in a large range of polar aprotic solvents, high thermal and mechanical resistance, chemical resistance on the entire range of pH and in oxidative medium, intrinsic biocompatibility, high permeability for low molecular weight proteins and high endotoxin retention ability [3]. Cyclodextrin is a cyclic oligosaccharide with amphiphilic nature due to the hydrophilic surface and the hydrophobic internal hollow [4]. Cyclodextrin could be used in the biomedical field because of its biocompatible and biodegradable properties [5]. In this work polysulfone membrane functionalized with cyclodextrin architecture were fabricated successfully via immersion of the commercial polysulfone in cyclodextrin solution. The morphologies and structure of the obtained composites membranes were investigated by scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FT-IR), Raman spectroscopy (Raman), X-Ray Photoelectron Spectroscopy (XPS). The SEM images showed that the PSF membrane pores were filled with cyclodextrin. In addition, the FT-IR and XPS results showed a successful functionalization of PSF membrane with CD structures for potential usage in drug delivery applications.

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Prostate on a chip

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In order to give greater assistance as well as more relevant results when changing human cells, researchers looked into appropriate options to animal experiments.
According to the report, the adoption of organ-on-a-chip technologies has surpassed educational institutions, due to a need to further understand the physiology of illness and wellness, as well as to seek innovative ways to enhance the human situation.
Furthermore, the development of such microfluidic devices known as "organs on a chip" ought to provide us with biological responses that are comparable to those shown inside living humans when exposed to various stimuli, which excites the field of science for a variety of reasons, particularly the potential future assurance of every medical therapy that may be assessed on them. Although this novel approach has been tested on numerous organs in the human body, it has only a limited applicability to the prostate, with the single research focusing on the aggressive phase of cancer.
Lastly, given the arguments indicated above, the aim of the project is to induce similar cellular activity as that found in the human prostate using organ-on-a-chip technology.

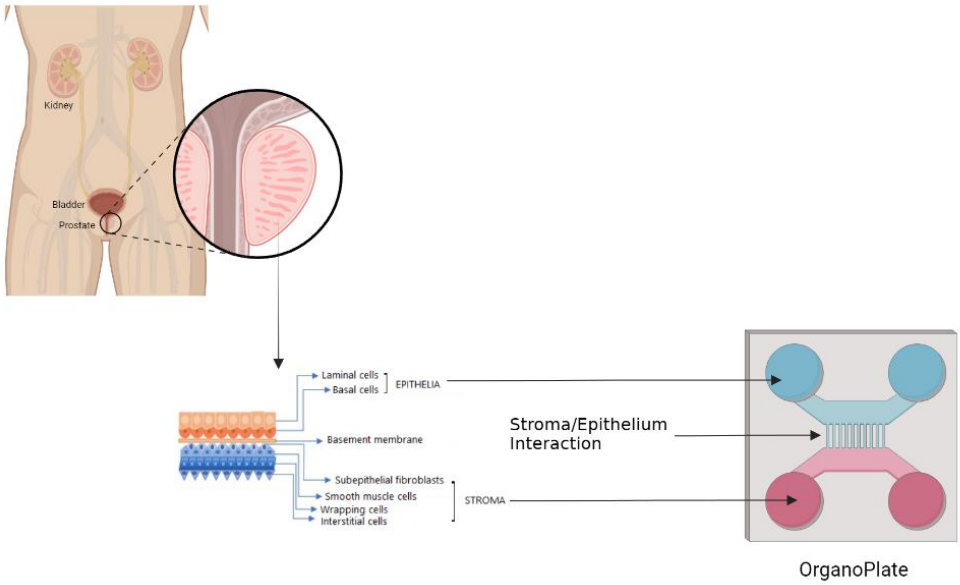

Figure 1. Localization and differentiation of prostate.

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Three-dimensional fibrous structures based on polymers as templates for copper oxide fiber webs

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Currently, the development of inorganic architectures using three-dimensional fibrous structures based on polymers as templates is studied intensively due to their potential applications in different areas such as optoelectronic devices, photocatalysis, chemical sensors, etc. Hence, inorganic fibrous structures featured by high surface area can be relative easily prepared by replicating the specific three-dimensional fibrous architecture of various organic templates offered by nature[1] or fabricated by electrospinning[2]. Versatile technique, electrospinning allows the fabrication of web-like structures based on polymers, further these can be used as templates for obtaining their inorganic replica. As regards inorganic semiconductors, copper oxide attracted considerable attention because it can be prepared in many morphologies by simple and relative environmental friendly routes that involve low-cost chemical reagents[3].

In the present study, copper oxide fiber webs were obtained by: i) immersion of natural templates based on eggshell membrane (bio-polymer featured by a three-dimensional porous interwoven fibrous protein network) in the metal salt aqueous solution and their further calcination and ii) fabrication of templates based on polymer fibers by electrospinning an aqueous solution of metal salt-polyethylene oxide-egg protein and their further calcination. The morphological, structural, compositional, optical and electrical properties of the obtained semiconducting fiber webs were evaluated. Regardless the chemical nature and the structure of the templates, each organic architecture is perfectly replicated into an inorganic one consisting in interconnected fibers formed by semiconducting nanoparticles. Moreover, during the calcination step, Si/SiO_2 patterned with interdigitated metallic electrodes were used as substrates for achieving the electrical paths between the neighboring grid structures.

Therefore, inorganic fiber webs with tailored morphology and functional properties can be designed employing three-dimensional fibrous structures based on polymers as templates. Furthermore, by combining the replication path and the interdigitated metallic electrodes patterns, devices based on three-dimensional semiconducting architectures can be straightforward fabricated.

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