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E4. Nanomaterials for Drug Delivery, Imaging and Immuno-Engineering

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SE4-O001
FABRICATION, OPTIMIZATION, AND CHARACTERIZATION OF SURFACE-DECORATED LIPOSOMES CO-ENCAPSULATING QUERCETIN AND PENETRATION ENHANCERS FOR TARGETED DELIVERY TO HEPATOCELLULAR CARCINOMA: IN-VITRO RELEASE AND CYTOTOXICITY STUDIES

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Hepatocellular carcinoma (HCC) is one of the most prevalent and leading causes of cancer-related death worldwide. Conventional chemotherapy is generally prescribed for HCC treatment; however, it demonstrates serious systemic side effects. Thus, it becomes critical to develop new alternative therapies for the treatment of HCC. The flavonoid quercetin (QR) has recently been recognized as a promising cancer chemopreventive agent, owing to its high potency and safety. However, its practical use is limited due to its low aqueous solubility and bioavailability. The current study aims to develop QR-loaded, surface-coated liposomes containing penetration enhancers for liver cancer-targeted drug delivery. Liposomes were prepared by the thin-film hydration method, followed by sonication. L-α-phosphatidylcholine and cholesterol in a ratio of 2:1 (w/w) were used to make the liposomes. Three penetration enhancers were studied: the non-ionic Pluronic® F-127, the anionic sodium deoxycholate (SDC), and the cationic cetyltrimethylammonium bromide (CTAB). The liposomal formulation containing CTAB demonstrated the best release and kinetic results. It was spherical in shape, with a particle size of 284.54 + 28.42 nm, polydispersity of 0.32 + 0.14, zeta potential of 20.20 + 10.61 mV, viscosity of 11.19 + 4.96 cP, encapsulation efficiency of 99.10 + 0.098%, drug loading capacity of 13.56 + 0.013%, and 86.50 + 0.54% drug release in 24 hours. This liposomal formulation was then coated with two different surface coating polymers: cationic chitosan to prepare chitosomes and non-ionic polyethylene glycol (PEG) to prepare PEGylated liposomes to increase cellular uptake and anticancer efficacy, and tested against hepatic HepG2 cells and other non-hepatic cancer cells, U937, and A549 cells. PEGylated liposomes with positively charged CTAB showed high cytotoxicity against HepG2 cells and increased cytotoxicity against U937 and A549 cells compared to free QR, uncoated liposomes with CTAB, and chitosomes, with IC_{50} values of 400 µM (HePG2), 350 µM (U937), and 300 µM (A549), respectively. These findings suggest that the delivery of QR-loaded, PEGylated liposomes containing CTAB as a penetration enhancer significantly control the severity of HCC and can be considered a promising multifunctional nanocarrier in the management of HCC and other cancer types.

Keywords: hepatocellular carcinoma, quercetin-loaded-coated liposomes, liver cancer-targeted drug delivery

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SE4-O003 Invited Talk

ELECTROSPUN QUERCETIN-LOADED HYBRID NANOFIBERS FOR VAGINAL COMPOUNDS DELIVERY: DESIGN, AND EVALUATION OF ITS PHYSICOCHEMICAL AND ANTICANDIDIASIS PROPERTIES

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Conventional strategies (creams, foams, gels, etc.) to treat vaginal candidiasis, lack effectiveness and provide low retention and distribution of therapeutic compounds in vaginal tract. Therefore, the present study is based on developing a film based on polymeric electrospun nanofibers, as a controlled release system of active ingredients in the vaginal tract, using quercetin, as a model molecule.

The free and charged nanofibers were created by modifications to the electrospun technique; the physicochemical properties (diameter, morphology, and zeta potential) of free and loaded systems were evaluated. Swelling parameters and in vitro release kinetics were also evaluated in simulated vaginal fluids. The antifungal capacity against strains of C. albicans (using ATCC strains and strains from clinical cases) was determined as well. The results showed that the fibers, both free and quercetin-loaded, have average diameters of 550 nm, with zeta potential of around -25 mV, and with a corrugated morphology. The fibers swell in a greater proportion in simulated vaginal fluids at pH related to the presence of microbial infection (pH 7.2) than at pH values considered healthy in the vaginal tract (5.0). The in vitro release kinetics in simulated vaginal fluids showed that the system releases around 70% of quercetin in 2 h at pH related to vaginal microbial infection (7.0); while at pH values of a healthy vaginal tract (pH 5.0), the release was slower, achieving a release of 40% of quercetin. On the other hand, free and loaded nanofibers had different effects on Candida strains; in ATCC strains, free and loaded fibers had the capacity to inhibit yeast growth by 50% and 70% (respectively), while in clinical case strains, the systems inhibited yeast growth by 55%. and 80% (respectively), after 4 and 8 h of incubation. This work indicates that the developed systems could have great potential to be applied as alternative antimicrobial therapies for vaginal health.

Keywords: nanosmart delivery systems, nanosmart delivery systems, nanosmart delivery systems

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SE4-O005

BIOMIMETIC PEPTIDE NANOTUBES : FROM AOMIC STRUCTURES TO DRUG RELEASE APPLICATIONS

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Slow molecule release is a challenge for many pharmaceutical drugs. We have investigated the structure/efficiency relationship in trade peptide gels for many years. Some structures of peptide nanotubes have been solved at the molecular or atomic scale. Lanreotide is an octapeptide that self-assembles in water into monodisperse supramolecular nanotubes, whose diameter and wall thickness are 244 Å and 18 Å, respectively. [Valery et al PNAS 2003]. These nanotubes can be used as a template to produce micron-long silica nanotubes with a monodisperse diameter [Pouget et al, Nature Mat. 2007]. The diameter of these nanotubes can be adjusted by a single mutation of the peptides [Tarabout et al, PNAS 2011]. Collaborators recently solved the atomic structure by cryo-EM [Pieri et al, PNAS 2022]. We also studied a pH-sensitive self-assembled peptide that forms either crystalline bundles of small nanotubes of 10 nm diameter (pH <6.5) or large nanotubes of 50 nm diameter (pH>7.5). [Valery et al, Nature Comm. 2015]. Two of these biomimetic self-assemblies are used in controlled delivery of active ingredients in many countries (AMM, FDA, etc.) as Somatuline and Decapeptyl.

Keywords: peptide, gel, nanotubes

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SE4-O007
THE IMPACT OF THE DESIGN OF MoO_3 NANOSTRUCTURES ON THE ANTIBACTERIAL BEHAVIOR

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Molybdenum trioxide (MoO_3) has emerged as a promising nanomaterial with antimicrobial properties that offer innovative solutions to address the growing threat of antibiotic-resistant bacterial infections and the proliferation of pathogenic microorganisms. In the present work, the synthesis of MoO_3 is evaluated through the differences in the crystallization induced by the reaction time and the antibacterial activity (AA) performance against Gram-positive S. aureus and Gram-negative E. coli in the function of the amount of the nanoparticles (8, 4, 2, 1 and 0.5 mg/ml). The results indicate that the nanofiber morphology presented in MoO_3 is attributed to the orthorhombic phase of nanoparticles. It was observed that crystallization times affect the diameter of the fiber and the Mo/O ratio at short crystallization times (12 h), obtaining a smaller fiber diameter as well as a lower proportion of Mo (molybdenum) respecting O (oxygen). As a result, high efficiency inhibits the growth of S. aureus and E. coli (close to 100%) compared to crystallization times, suggesting the potential application as an antimicrobial agent to address important problems related to bacterial infections.

Keywords: molybdenum trioxide, crystallization, antibacterial activity

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SE4-O008 Invited Talk
UNVEILING SENSITIVITY: EXPLORING NANOPARTICLE INTERACTIONS IN 2D AND 3D CELL MODELS FOR NEW CONCEPTS IN NANOTOXICOLOGY

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Two-dimensional (2D) cell culture monolayers are employed in toxicological evaluations of nanomaterials, but their simplicity in handling comes with limitations stemming from structural and complexity disparities compared to three-dimensional (3D) in vitro cell models, like spheroids. This work delves into a comparative nanotoxicological exploration conducted on fibroblast (L929) and melanoma (B16-F10) cells cultivated in both two-dimensional (2D) and three-dimensional (3D) arrangements. The focus is unveiling the differences in cytotoxicity, reactive oxygen species (ROS) production, genotoxicity, cell morphology complexity, and nanoparticle uptake between these culture architectonics.
Silver nanoparticles (AgNPs), known for their wide-ranging applications, exhibit higher cytotoxicity in spheroids than monolayer cultures. Moreover, the apoptotic cell percentages and ROS production register higher levels in the 3D cell culture, indicating heightened cellular responses in such environments. A notable disparity emerges in the concentration requirements of AgNPs to induce considerable DNA damage, with 2D cultures necessitating twice the concentration compared to their 3D counterparts. This discrepancy underscores the enhanced sensitivity of spheroids to the genotoxic effects of AgNPs, signifying the imperative of considering diverse cellular architectures in nanotoxicity assessments. Conversely, folic acid-functionalized upconversion nanoparticles (FA-UCNPs) exhibit negligible toxicity across 2D and 3D models, underscoring their potential as biocompatible nanomaterials. AgNPs induce cytotoxic effects and prompt the disaggregation and downsizing of spheroids in a concentration-dependent manner, highlighting the dynamic interplay between nanoparticles and cellular structures. In contrast, FA-UCNPs exhibit enhanced internalization in spheroids, emphasizing the intricate effects of nanoparticle-cell interactions within 3D microenvironments.
These findings show the pivotal role of spheroids as a more sensitive model for assessing nanoparticle biocompatibility and internalization dynamics. This research enriches our understanding of nanotoxicology by bridging the gap between 2D and 3D cell cultures. It underscores the importance of tailored experimental frameworks in evaluating the safety and efficacy of novel nanomaterials.

Keywords: Nanotoxicology, Spheroids, Biocompatibility

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SE4-O009
SYNTHESIS AND ANTICANCER ACTIVITY OF INDOMETHACIN-LOADED JANUS DENDRIMERS

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Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly known because of their use in treatment of pain, fever, and inflammatory diseases. NSAIDs inhibit the activity of COX-1 and COX-2, which are the enzymes involved in inflammatory process. In recent years, several studies report that these enzymes are overexpress in cancer cells. In this way, some NSAIDs have been repurposed in cancer treatment and having excellent results of their anticancer activity. In order to improve the properties of drugs, such as biopermeability, water solubility and biocompatibility; novel vehicles have been developed. One of these new structures are Janus dendrimers which are monodisperse asymmetric hyper-branched nanomolecules that have promising application in nanomedicine. Here, we report the synthesis and anticancer activity of a series of indomethacin water-soluble Janus dendrimer conjugates. Briefly, indomethacin was coupled to a diethanolamine dendron and, after a deprotection reaction, coupled to triethyleneglycol. On the other hand, the dendron was prepared from Behera's amine and succinic anhydride. Finally, both dendron were linked by a Steglich esterification reaction. G1 and G2 dendrimer were obtain and reacted with formic acid to obtain three carboxylic acids at the periphery which were then transform into their sodium salts obtaining the amphiphilic water-soluble Janus dendrimers loaded with two or four indomethacin moieties. Anticancer activity of dendrimers was tested obtaining good results against four cancer cell lines (PC-3, K562, HCT-15, MCF-7).

Keywords: Janus dendrimers, Indomethacin, Water soluble

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SE4-O010
TARGETING NANOFORMULATION FOR TREATMENT OF DIABETES MELLITUS

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Diabetes Mellitus (DM) is one of the fastest growing diseases worldwide. The pancreas is the organ most affected, particularly the pancreatic islet, specifically beta cell, which is responsible to produce insulin as the major glucose regulator. This is why a targeting nanosystem has been developed, based on poly (lactic-co-glycolic acid) PLGA nanoparticles (NPs) and a peptide capable of targeting a peptide receptor to perform a specific delivery and controlled release. NPs were optimized for their best physicochemical properties for use in beta pancreatic cells obtaining a hydrodynamic diameter of 198 ± 17.09 nm, zeta potential -27.66 ± 3.40 mV, and 12.05 ± 3.20 % w/w functionalization onto the surface of the NPs. The peptide in NPs were also identified by NMR spectroscopy. Thus, the NPs were tested for their internalization and association in pancreatic islets.

Keywords: Targeting NPs, Drug delivery, Pancreatic islets

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SE4-O011
1D AND 2D INORGANIC NANOMATERIALS AS DOXORUBICIN CARRIERS FOR CANCER TREATMENT

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Inorganic metal oxide nanomaterials are emerging as good candidates for the delivery of a range of chemotherapeutic drugs. Herein, halloysite nanotubes clays (HNT), hydrogen titanate nanotubes (TNT), aluminum oxide nanowires (ANT) and titanium dioxide nanosheets (TNS) are evaluated as drug nanocarriers, using doxorubicin (DOX) as a model therapeutic compound for cancer treatment. The materials were sonicated in distilled water at 140W for 90 min and then the samples were centrifugated to ensure a nanoparticle size lower than 500 nm. The nanomaterials were characterized by XRD, ATR-FTIR, TEM, N_2 adsorption-desorption isotherms at -196°C, and TGA, which revealed for TNT and ANT remarkably high surface area (S_{BET} approx. 180 m^2/g) while HNT and TNS a low surface area (S_{BET} approx. 50 m^2/g). All the materials displayed mean nanoparticle sizes between 50 – 100 nm. The nanoarriers showed a moderate loading efficiency for the encapsulation of DOX. The carriers showed pH-dependent release of DOX and adjust their release profile at first-order kinetic model. The release at pH = 5.5, for all the nanocarriers, was faster than that at pH = 7.4. Additionally, hemolysis assays indicated that TNT, ANT and TNS was a biocompatible nanocarrier with no toxicity, whereas HNT was toxic even at low dosages for both red blood cells. In vitro experiments with HeLa cells confirmed the non-cytotoxicity of 100-300 µg mL^{-1} nanomaterials after 24 h of incubation. The chemotherapy assays confirmed the DOX release capacity a cell viability lower than 70% for all the tested materials after 24 h of incubation.

Keywords: Biocompatible nanomaterials, Drug delivery, Inorganic materials

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SE4-O014
VIRUS-BASED BIONANOREACTORS FOR SPECIFIC COLON CANCER CELLS ANNIHILATION

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Today colon cancer is a highly frequent type of cancer. It is well known that this type of cancer cells express the carcinoembryonic antigen (CEA) and are anchored in the cell surface. The aim of this project consists of the design and production of virus-based bionanoreactors with glucose oxidase catalytic activity for specific colon cancer cells by CEA antigen recognition. First, the synthesis of bionanoreactors will be performed by glucose oxidase enzyme (GOx) encapsulation into the Bromo mosaic virus (BMV) virial capsid using the self-assembly conditions. Then, the encapsulated GOx active enzyme in BMV capsid or GOx bionanoreactor will be functionalized with the antibody anti-CEA to drive the bionanoreactor to specific colon cancer cells. The antibody anti-CEA will be anchored in the external surface of bionannoreactors for cancer cell CEA antigen recognition. Finally, the specific cytotoxic effect of anti-CEA bionanoreactors will be studied using colon cancer cell lines. The cytotoxicity activity of the virus-based GOx bionanoreactors in colon cancer cells will be discussed.

Keywords: Glucose oxidase (GOX), Antibody anti-CEA, Bionanoreactors

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SE4-O015
SYNTHESIS OF ZrO_2:Yb^{3+}-Tm^{3+} NANOPARTICLES COATED WITH SiO_2 FOR THERANOSTIC APPLICATIONS IN LUNG CANCER

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Lung cancer is one of the most common types of cancer and the one that causes the most deaths in the world. This disease is commonly treated with chemotherapy treatment. However, this medical procedure is not selective and damages healthy and cancerous cells. Theranostics is an alternative to treat this cancer, a recently created field of nanomedicine that incorporates diagnosis and treatment methods on the same platform. Therefore, in this research, a SiO_2-coated ZrO_2:Yb^{3+}-Tm^{3+} upconversion nanoparticle platform was synthesized using the sol–gel method. The core–shell nanoparticles were analyzed by scanning electron microscopy (SEM), X-ray diffraction (XRD), infrared spectroscopy (FT-IR), 975 laser excitation fluorimetry, and infrared camera to determine the photothermal properties. The results showed the formation of ZrO_2:Yb^{3+}-Tm^{3+}@SiO_2 nanoparticles with emissions in visible and IR regions due to different energy levels of Tm^{3+}. Furthermore, the study of photothermal properties showed a suitable temperature increase of up to 46 °C for lung cancer treatment. Therefore, this platform will be functionalized with TGA for bioconjugation with the Cetuximab® antibody for detecting epidermal growth factor receptor (EGFR)-mutant lung cancer, which is suitable for theranostic applications.

Keywords: Lung cancer, Up-conversion nanoparticles, Theranostic applications

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SE4-O016
EXPLORING THE ANTIOXIDANT AND CYTOTOXIC EFFECTS OF RARE EARTH-DOPED ZNO NANOPARTICLES: IMPLICATIONS FOR BIOMEDICAL APPLICATIONS

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In this work, ZnO-NPs were doped with La^{3+} and/or Sm^{3+} and were synthesized by the sonochemical method. The materials were tested for cytotoxicity using colon cancer (HT29) and breast cancer (MCF7) cell lines, respectively. Both cell lines were assessed for their ability to reduce the production of reactive oxygen species (ROS), and their antioxidant activity was examined. The capacity to decrease the generation of reactive oxygen species (ROS) was tested in both cell lines, whereas their antioxidant activity was investigated using the DPPH assay. These nanomaterials had a cytotoxic effect on MCF7 cells, resulting in the death of 10.55–42.54% of the cells, while they caused the death of 18.23–38.64% of the cells in the HT29 cell line. These things happened because they were able to suppress the production of reactive oxygen species (ROS) in the two cell lines, which caused them to die. Z, ZL, ZLS, and ZS demonstrated the highest ability to scavenge DPPH free radicals at 45.91, 117.35, <2.5, and 95.28 mg/mL, properly. Machine learning was used to validate the bioactivities of the recorded nanomaterials. The information produced by this work advances our understanding of rare-earth-based nanomaterials and their potential uses in medicine

Keywords: Rare earth, Antioxidant, Cytotoxic

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SE4-O017 Invited Talk
ADVANCES OF A BIOPOLYMERIC NANOFORMULATION AIMED FOR CARDIOMETABOLIC DISEASES

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Heart failure (HF) is the leading cause of death in industrialized nations. It is classified in several categories, being that metabolic nature, denominated HF with preserved ejection fraction (HFpEF), prevalent in more than 50% of the cases. Currently it has limited therapeutic options, with mild clinical success. HFpEF is characterized by a cardiac inflammatory environment, a characteristic that could be exploited for drug delivery. In this project, an inflammatory-sensitive nanosystem was developed, based on biocompatible materials, including poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) and a coating capable of sensing inflammatory signals such as pH alterations, with the objective to achieve site-specific controlled and sustained drug delivery in cardiac pathophysiological conditions of HFpEF. In this presentation, the advances of the inflammatory-sensitive nanosystem development will be presented, showing proof concept of increased sensitivity (3x) under acidic conditions, and a time-dependent faster association of the nanosystem to cardiac cells (H9c2) under inflammatory conditions.

Keywords: drug delivery, pH, cardiometabolic disease

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SE4-O018
ELABORATION AND CHARACTERIZATION OF POLYMERIC MEMBRANE FOR OPEN WOUND TREATMENT

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INTRODUCTION: The polymer biomaterials has become a very interesting area for research in the development of macromolecules, due to their use as cardiovascular therapeutic devices, skin substitutes and drug delivery systems [1]. An example are the polymer nanofibers, which have been used in tissue engineering, biosensors, pharmaceutical, electronic devices, filters, and drug delivery systems [2]. Polymeric nanofibers, uniaxial poly-e-caprolactone, biocompatible and biodegradable polymer, was synthesized. OBJECTIVE: Obtain prolonged delivery dug system of poly-e-caprolactone loaded with propolis as antibacterial film to treatment of open wounds. METHODOLOGY: Electrospinning device: The system was ensemble with pieces bought in ecommerce stores. Synthesis of nanofibers: 0.5g of poly-e-caprolactone with 50 µL of propolis was dissolved in 3mL of acetone. The prepared solution was filled into a syringe and pushed with a constant flow and voltage of 15 kV. Nanofibers were collected from an aluminum sheet. Microbicidal activity was evaluated against Staphylococcus aureus. RESULTS: A polymeric film of poli-e-caprolactone/propolis was obtained. The mean diameter of nanofibers was of 850 nm. The microbicidal activity was more efficient than the poli-ecaprolactone/propolis solution. CONCLUSIONS: The electrospinning technique allowed us to synthesize a polymeric film as an alternative for the treatment of open wounds. KEY WORDS: polymeric nanofibers, open wounds, drug delivery. REFERENCES: [1] Rojas Cortés, Manuel Guillermo; Vallejo Díaz, Bibiana Margarita; Perilla, Jairo Ernesto. (2008). Los biopolímeros como materiales para el desarrollo de productos en aplicaciones farmacéuticas y de uso biomédico. Ingeniería e Investigación, vol. 28, no 1, p. 57-71. [2] Aganwal, S.,Wend

Keywords: POLYMERIC NANOFIBERS, OPEN WOUND TREATMENT, DRUG DELIVERY

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SE4-P001
CARBON QUANTUM DOTS AS THERANOSTIC AGENTS FOR PHOTOTHERMAL THERAPY AND SIMULTANEOUS FLUORESCENT IMAGING

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Theranostic agents are biomaterials that are characterized by having dual functionality to diagnose, monitor and treat diseases simultaneously. One of these applications is diagnosis to obtain fluorescent images both in vitro and in vivo and the other application is the treatment against different diseases, one of them, cancer. Recent research is focusing on improving the efficiencies of these agents with just one application through chemical modifications and bioconjugation selectively and specifically at the tumor site, eliminating and/or reducing the side effects of conventional treatments. That is why CQDs were synthesized by microwaves and characterized using DLS, XRD, IR, UV-Vis and photoluminescence methods. It is desired to continue research by functionalizing this material with the PSG1 antibody, to explore its diagnostic capabilities by producing fluorescent bioimages and its therapeutic property by converting NIR light into thermal energy to generate localized heat (phototherapy). All this to assess the specificity and effectiveness of the PSG1-CQDs bioconjugate as a theranostic agent in cells with expression of the carcinoembryonic antigen in vitro and photoirradiate it at a specific length to induce a phototherapeutic.

Keywords: Quantum dots, Carbon, Theranostic agents

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SE4-P004
HALLOYSITE-TOLUIDINE BLUE O NANOCOMPOSITES AS DUAL DRUG DELIVERY AND VISIBLE LED LIGHT-SENSITIVE CARRIERS FOR ENHANCEMENT IN CANCER CHEMOPHOTOTHERAPY

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The photosensitization of halloysite nanotubes (HNT) was investigated with the photosensitizer toluidine blue O (HNT@TBO), with the aim to obtain new drug nanocarriers with potential application in combined therapy for cancer treatment. The materials were characterized by Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), transmission electron microscopy (TEM) and nitrogen adsorption-desorption isotherms at -196°C where the successful functionalization of the HNT's surface with every photosensitizer was demonstrated. In addition, photochemical characterization was carried out through fluorescence spectroscopy – using specific scavengers for singlet oxygen ($^1O_2$) and hydroxyl radical (HO•) – and electron paramagnetic resonance (EPR) where it is evident that pristine HNT is not capable to produce reactive oxygen species (ROS) while HNT@TBO produce ROS under irradiation with cold white LED light at 150 W/m^2. All materials showed loading and release capacity of doxorubicin (DOX), as model chemotherapeutic drug. The cytotoxic effect of the nanocarriers on the HeLa cancer cell line was evaluated in chemotherapy, photodynamic therapy and photochemotherapy, obtaining that the nanocarriers without drug and in darkness do not displayed cytotoxicity. In the case of chemotherapy, it was observed that all show a similar trend in order to reach the minimum viability at concentrations above 100 mg/L. In the case of photodynamic therapy, it was found that the effect is much more marked, achieving zero activity in the case of pristine HNT and significant phototoxicity of the HNT@TBO. Finally, the combined therapy showed a synergistic effect only for the HNT@TBO material reaching viability values comparable to the death control at concentrations of 50 mg/L.

Keywords: Halloysite, Chemotherapy, Photodynamic therapy

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SE4-P005
SYNTHESIS OF AMPHIPHILIC JANUS DENDRIMERS AS CHLORAMBUCIL NANOCARRIERS

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Janus dendrimers are novel nanostructures made of two different parts which are, ideally, complementary. In this way, it is possible to build structures with hydrophobic and hydrophilic scaffolds taking advantage of their properties. In this work, we report the synthesis of amphiphilic Janus dendrimers as nanocarriers for drug delivery. The hydrophobic part consists of diethanolamine dendrons loaded with chlorambucil, an anticancer drug, by a covalent bond. These dendrons (with two or four chlorambucil moieties) were synthesized by an alternated sequence of coupling and deprotecting reactions, Steglich esterification as the former and acid deprotection as the latter. On the other hand, the hydrophilic part was obtained from Behera's amine in its sodium carboxylate form. This dendron was synthesized from nitromethane and tert-butyl acrylate, and then the nitro group was reduced to amine and reacted with succinic anhydride. Finally, both dendrons were linked to obtain G1 and G2 Janus dendrimers with tert-butyl esters as end groups which were then transform into carboxylic acids and, finally, into sodium carboxylates. G1 and G2 Janus dendrimers were water soluble in its sodium salt form. These dendrimers could have potential use in biomedical applications as anticancer agents.

Keywords: Janus dendrimers, Chlorambucil, Water soluble

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SE4-P007
ROLES OF NANOSTRUCTURED BETA TRICALCIUM PHOSPHATE ON HUMAN MACROPHAGES BEHAVIOUR

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The host immune response plays an important role in determining the fate of synthetic grafts for bone healing. Studies demonstrated that calcium deficient hydroxyapatite (CDHA) is biocompatible, promotes bone repair in vivo, and even induces the formation of bone intramuscularly. In fact, there is evidence that the nanostructure of CDHA can modulate the immune response of macrophages and in turn, stimulate the osteogenic capacity of osteoblasts. Here, we studied the effect of micro and nanostructure of CaP ceramics on the behaviour of macrophages, independently of the effects of the chemical composition. We fabricated a monolithic nanostructured β-TCP (N-β-TCP) that replicates the nanostructure of calcium deficient hydroxyapatite (CDHA) in a process that mimics the embryologic development of bones. First, the hydrolysis of the α-TCP powder into CDHA was performed in water at 37 °C. Then, β-TCP and N-β-TCP were obtained by sintering the CDHA at high and low temperature, respectively. The physical and chemical characterization of materials were performed by XRD and SEM. To study the influence of microstructure on cell behaviour, macrophages were obtained from buffy coat, and they were cultured on CDHA, β-TCP, and N-β-TCP. Cell metabolic activity, DNA quantification,

morphology, and polarization to M1 and M2, were determined at different timepoints. XRD results showed a successful synthesis of the nanostructured material (N-β-TCP) by the dehydration of CDHA, and SEM images confirmed the nano-topographical morphology. Cell cultures revealed higher metabolic activity and elongated morphology with several lamelopodia and filpodia, of macrophages in contact with N-β-TCP. Also, immunostaining revealed highest level of Arg-1 in macrophages seeded on N-β-TCP. Therefore, the replication of the nanostructure of CDHA in N-β-TCP allowed the adhesion of macrophages up to 7 days.

Keywords: nanostructure ceramic, macrophage, cellular behaviour

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SE4-P008
BIODEGRADABLE DENDRIMERIC NANOCARRIERS AGAINST HUMAN CHRONIC MYELOGENOUS LEUKEMIA

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Janus dendrimers are systems with broken symmetry, unlike conventional dendrimers which are highly symmetrical. Janus dendrimers are synthesized from two dendrons joined through a nucleus. Both dendrons have different properties, which may or may not be complementary, resulting in a multifunctional molecule.

In the present research work, the design and synthesis of a biodegradable Janus dendrimer conjugated with acemetacin was carried out, using a simple methodology, through two types of reactions: protection-deprotection and esterification, from the 2,2-bis(hydroxymethyl) propionic acid (Bis-MPA), One of the dendrons with a group azide as a focal point and four hydroxyl groups as terminal group, and the second dendron with an alkyne group as a focal point and four molecules of acemetacin as terminal group. The Janus dendrimer was obtained by a Click-type azide-alkyne reaction catalyzed by CuI(I). All the compounds obtained were characterized by NMR in one and two dimensions and mass spectrometry. From the analysis of the spectroscopic data, it can be concluded that a Janus dendrimer with four terminal hydroxyl groups in one dendron and four acemetacin molecules in the other dendron was synthesized for the first time. Anticancer activity studies were carried out on the dendrons and Janus dendrimer against six cancer cell lines and it was observed that the Janus dendrimer was active and selective against human myelogenous chronic leukemia cancer cells.

Keywords: Janus dendrimers, acemetacin, leukemia cancer

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SE4-P009
DENDRIMERIC NANOCARRIERS WITH MELPHALAN AGAINST HUMAN BREAST CANCER CELLS

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In recent years, macromolecules such as Janus dendrimers have been used in drug delivery to improve solubility, membrane permeability, and decrease side effects. The well-defined structure of dendrimers with multiple peripheral functional groups allows drug conjugation via covalent bonds. Janus dendrimers with aliphatic polyesters are among the most studied class of materials due to their biodegradability, biocompatibility, and low toxicity.
In the present work, the synthesis of a Janus-type dendrimer conjugated with melphalan (a commercial anticancer drug that intercalates DNA and is insoluble in water) is presented. The two dendrons were synthesized from 2,2-bis(hydroxymethyl)propionic acid (Bis-MPA) and tris(hydroxymethyl)aminomethane (Tris), one dendron with an azide as a focal group with melphalan as a terminal group and the other dendron with an alkyne group as a group focal with hydroxyl groups as terminal groups. The two dendrons were coupled to obtain the Janus dendrimer through an azide-alkyne Click reaction. The dendrons and dendrimers were characterized by one- and two-dimensional NMR. The anticancer activity of the Janus dendrimer against six cancer cell lines was studied and showed high activity against breast cancer.

Keywords: Janus dendrimers, melphalan, anticancer activity

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SE4-P010
SURFACE FUNCTIONALIZATION OF FLUORESCENT NANODIAMONDS (FNDs) FOR BIOMEDICAL APPLICATIONS

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Nanodiamonds (ND), nanometer-sized carbon structures, have exceptional chemical, optical and biological properties. In particular, nanodiamonds (NDs) are characterized by their biocompatibility, low toxicity to cells, chemical inertness, large surface area relative to their volume, and small size, allowing them to have potential value for medical and biological applications. Fluorescent nanodiamonds (FNDs) have revolutionized research and innovation in cell imaging and tracking, showing great promise as drug delivery vehicles, fluorescent markers, protein transport, and in technological applications such as fiber optic technologies.
In this work, the surface of nanodiamonds was modified by the ultrasonic method and the addition of an extract of the medicinal plant Cissus Genus in order to improve their luminescent properties. The optical properties of such nanodiamonds placed in aqueous suspensions were studied and compared with the resulting classical detonation nanodiamonds. To obtain nanodiamonds functionalized with Cissus Genus plant extract, NDs were treated by one of the following methods: 1) mixing with a solution distilled water and 30% hydrogen peroxide in several ratios, 2) bubbling ozone, 3) mixing with theraphthal (soluble cobalt phthalocyanine containing -COONa groups) aqueous solution, 4) mixing with theraphthal and urea. Then, the formed mixtures were subjected to ultrasonic treatment (35 kHz) for 1-12 hours. Finally, the samples were washed with distilled water and Cissus Genus extract was added to the resulting samples in different quantities. The formed nanoparticles were characterized by FTIR spectroscopy, UV-visible spectroscopy, scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The presence of red

luminescence was observed in NDs functionalized with an extract of the Cissus Genus plant (nanoparticle size of 4-7 nm). The resulting nanostructures are non-toxic and can be used to develop more effective and selective drug delivery systems, including fluorescent markers.

Keywords: Nanodiamonds, Fluorescence, Theraphthal

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SE4-P013
ELABORATION AND MICROBIOLOGIC EVALUATION OF POLYMERIC NANOCAPSULES TO ACNE TREATMENT

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INTRODUCTION: In recent times, the vehicles used in cosmetics have improved and innovated penetration into the different layers of the skin, limiting permeation and preventing systemic absorption of drugs. Nanocapsules with a diameter of 200 to 500 nm possess a typical shell-core structure, where the drug is confined to a reservoir or cavity surrounded by a membrane or polymeric coating. They are vehicles used to deliver the encapsulated material to deeper layers of the skin and have shown maximum deposition of the active ingredient content in the deeper layers of the skin, making them ideal for the treatment of acne.
OBJECTIVE: Design, synthesize and characterize a pharmaceutical system with nanocapsules to include them in a topical formulation for the treatment of acne.
METHODOLOGY: Diffusion-emulsion method. It begins with a presaturation of the organic solvent and water in a separatory funnel. Then, in separate flasks, the organic phase and the aqueous phase are prepared by dissolving the corresponding materials in each. The phases are mixed and emulsified under high speed homogenization (10,000 rpm). The diffusion stage is obtained by adding excess water to the emulsion. The organic solvent was then removed and the suspension was concentrated under reduced pressure.
RESULTS: PCL nanocapsules with a size of approximately 200 nm to 500 nm were obtained. Microbial activity was more efficient and prolonged, eliminating 100% of bacteria (Propionibacterium acnes)
CONCLUSIONS: The emulsion-diffusion method allowed the synthesis of polymeric nanoparticles as an alternative for the treatment of acne.

Keywords: POLYMERIC NANOCAPSULES, ACNE TREATMENT, Propionibacterium acnes

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SE4-P015
CYTOTOXICITY AND BIOCONJUGATION STUDIES OF NANOPARTICLES BY UPCONVERSION FOR DETECTION OF BREAST CANCER BY CONFOCAL MICROSCOPY

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Bioimaging based on UCNP upconversion nanoparticles offers a unique approach, by the use energy at infrared spectrum region as an excitation source; they have many advantages for bioimaging, such as the absence of autofluorescence, low phototoxicity and improving the depth of penetration into tissues. There are reports where they proposed as an alternative treatment for cancerous tumors. The cytotoxic effect of UCNPs on healthy cells measured using leukocytes. Cells seeded at a density of $1x10^6$ in 24-well plates in 500 µL of supplemented RPMI medium. The UCNPs were previously dissolved in RPMI and then added at different concentrations (50, 100, 200, 400 and 800 µg) to the plate. The interaction of UCNPs with cells incubated for 4 and 24 hrs at 37 °C with 5% CO_2. After the incubation period, viability was analyzed by bright field microscopy, using trypan blue and propidium iodide with the floid cell imaging station using an LED-based excitation source with a wavelength of 646/68 nm. For the cell viability assay, cell viability greater than 85% obtained for both cases. The cell viability values shown present a low cytotoxicity, taking into account that the nanoparticles used were uncoated, making a comparison with the coated ones, an increase in cell viability is observed when adding the SiO_2 coating that generates the biocompatibility of the UCNPs and allows having an adequate interface for bioconjugation. Through chemical synthesis, 1,1'-carbonyldiimidazole (CDI) was used to functionalize the hydroxyl groups of the UCNP@SiO_2 with the acylimidazole leaving groups of the CDI. For the bioconjugation of the functionalized UCNP@SiO_2-CDI, two proteins were used, a reference protein (BSA) and a binding protein (SBA). Nanoparticles bioconjugated with SBA obtained, which can specifically bind to N-acetylgalactosamine and β-D-galactose receptors of mouse breast cancer 4T1 cells. Immunofluorescence imaging performed on 4T1 mouse breast cancer cells.

Keywords: Bioimaging, nanoparticles, cytotoxic

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SE4-P017
MICROFLUIDICS ASSISTED SYNTHESIS OF NANOGELS FOR PHOTODYNAMIC THERAPY

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Nanogels have emerged as promising candidates for drug delivery systems in photodynamic therapy (PDT) due to their unique properties such as biocompatibility, tunable size, and high loading capacity. In this study, we present a novel approach utilizing microfluidics for the precise synthesis of nanogels tailored for PDT applications. The microfluidic platform offers precise control over reaction parameters, resulting in uniform

size distribution and enhanced reproducibility of the synthesized nanogels. The synthesis of nanogels comprises Tannic Acid (TA), Polyvinyl alcohol (PVA), and Sodium Alginate (SA), employing boric acid and calcium chloride (CaCl2) as crosslinking agents. The incorporation of TA as a part of the nanoparticle formulation introduces antibacterial properties to the nanogel, allowing for potential applications in wound healing as well as in the biomedical and pharmaceutical fields. Furthermore, the incorporation of photosensitizers, such as Au nanoparticles within the nanogel matrix, enables them to generate near IR light-induced reactive oxygen species (ROS). This microfluidics-assisted synthesis presents a significant advancement in the development of nanogel-based platforms for PDT, offering improved therapeutic outcomes and potential clinical translation.

Keywords: Nanogels, Photodynamic therapy, Microfluidic device

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SE4-P018
STUDY OF THE ADSORPTION OF DEXAMETHASONE ON IRON NANOPARTICLES STABILIZED WITH GLYCINE.

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The functionalization of the surface of magnetic nanoparticles (MNP) reduces toxicity, increases the surface area, and provides a certain surface charge that improves their stability. The glycine is an amino acid that in solution it is found as a dipolar ion that allows its interaction with the MNP and, due to its biological nature, improves the biocompatibility. In this work we present the results of the synthesis and characterization of Fe nanoparticles (NPs-Fe) and glycine functionalized at different concentrations. These samples were used as adsorbents for dexamethasone (DEX) which is a drug used in the treatment of COVID-19.
The NPs-Fe were synthesized by chemical reduction. The results of the characterization performed by Scanning Electron Microscopy (SEM), Potential Z (PZ), X-Ray Diffraction (XRD) and Fourier Transform Infrared Spectroscopy (FTIR) of NPs-Fe unstabilized and stabilized with glycine at concentrations of 0.16, 0.32 and 0.48 M are reported.
All samples of the NPs-Fe presented quasi-spherical morphology and with average diameters between 121 nm to 85.6 nm. The results showed that glycine improves the stability of NPs-Fe.The stabilized and unstabilized NPs-Fe exhibit a BCC crystal structure and the crystallite size decreased from 9.55 nm to 5.54 with the use of the glycine.
Furthermore, the adsorption kinetics are studied by varying the mass of the adsorbent (NPs-Fe) and keeping the concentration of the adsorbate (DEX) constant. According to the results obtained by UV-Vis spectroscopy, it is observed that the use of glycine improves the adsorption of the DEX on the surface of NPs-Fe.

Keywords: Iron nanoparticles, Glycine, Dexamethasone

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SE4-P019

DEVELOPMENT AND CHARACTERIZATION OF A SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM FOR A POORLY SOLUBLE BIOACTIVE COMPOUND.

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To solve the problems of solubility and bioavailability of bioactive compounds, nanotechnology offers the design of encapsulation systems such as self-nanoemulsifying drug delivery systems (SNEDDS). These systems are composed of molecules that allow self-assembly due to their chemical affinity, favoring the formation of nanomicelles using low energy techniques, which makes it more affordable than other processes. A 3^3 factorial design was carried out to obtain nanoemulsions with particle sizes less than 100 nm and a polydispersity index (PDI) below 0.2. These characteristics are sought in order to reduce the risk of having systems that tend to develop instability over time. Subsequently, the autonanoemulsification zone was delimited using a pseudoternary diagram. Nanoemulsions were obtained with particle sizes of 14.6 to 83.8 nm and PDI of 0.077 to 0.199. A Box-Behnken optimization design was carried out to identify the optimal values of each independent variable: bioactive compound, surfactant, and co-surfactant of our formulations that allowed to reach the lowest value of each of the dependent variables evaluated (particle size and PDI). FT-IR spectrograms were obtained showing that there are no changes in the structure of any compound, which is favorable for maintaining the bioactivity of our compound of interest. On the other hand, the centrifugal stability of the nanoemulsions was evaluated by subjecting them to centrifugation cycles from 4000 to 8000 rpm; none showed instability. Finally, three nanoemulsions with different formulations were subjected at three different temperatures: 5, 19, and 37 °C for 63 days. During this period, particle size and PDI as response variables were monitored to identify possible instability. As a result from this evaluation, we identified the appropriate temperature for its conservation and the most stable nanoemulsion to continue its evaluation.

Keywords: Nanoemulsions, SNEDDS, Stability

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SE4-P020
DESIGN AND SYNTHESIS OF ZNO QUANTUM DOTS-THEOPHYLLINE FOR HEPATOPROTECTIVE TARGETING NANOSYSTEM DELIVERY AND ITS EVALUATION IN RATS

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Medications are capable of preventing or curing diseases; however, all of them have the potential to cause side effects or adverse effects due to their prolonged use. This results in a less viable future, which can be harmful for those who suffer the disease, as they not only have to treat the condition with new medications,

but also must consume them in greater quantities to treat the conditions caused by the side effects. In the case of non-alcoholic steatohepatitis (NASH), a change in diet is often recommended as a treatment, but this is not always enough to control or cure this condition.
Therefore, this project seeks to create a synergy between two compounds: the ZnO with antimicrobial, antioxidant, antidiabetic, and angiogenesis properties, as well as good biocompatibility, stability, and the ability to be functionalized for selective drug delivery at the nanoscale; and theophylline, which has shown beneficial effects on liver damage.
The objective of this work was to develop a nanosystem using quantum dots functionalized with theophylline. As a first step, we design the nanosystem through molecular simulation, using Conceptual Density Theory (CDFT), which allowed us to study the interaction of quantum dots with theophylline. Then, we moved on to the experimental development of the synthesis of ZnO quantum dots, where dihydrated zinc acetate was used as a precursor agent and monohydrated lithium hydroxide was used as a reducing agent, followed by functionalization with theophylline. After that, the characterization of the quantum dots and nanosystem was carried out using UV-Vis, FTIR and DLS techniques, where the interpretation of the absorption peaks was carried out to verify the proposed interaction in the simulation and experimental calculations. In the last stage, the effect of the ZnO-theophylline nanosystem on CCl4-induced NASH was evaluated in male Wistar rats by determining biochemical and histological markers to test its hepatoprotective activity.

Keywords: Nanosystem, Drug-delivery, Liver

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SE4-P021
ASSOCIATION OF COLISITIN WITH NANOLIPOSOMES COATED WITH CHITOSAN TO CONFRONT PANDRUG RESISTANT BACTERIA.

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Bacterial resistance is a serious public health problem worldwide since the genes responsible for it are easily disseminated among bacterial populations while the search for new antibiotics is a delayed process. Currently, there are bacteria resistant to all antibiotics used in clinical practice known as pandrug-resistant bacteria (PDR), including colisitna, a lipopeptide used as a last resort to treat infections caused by Gram-negative bacteria. In this way, nanotechnology has emerged as an alternative to recover the biological activity of conventional antibiotics. In this study, colistin was associated with chitosan-coated nanoliposomes. The size, Z potential and polydispersity were characterized. Subsequently, the antibacterial activity of the nanoformulation was evaluated against a susceptible and three PDR strains of Pseudomonas aeruginosa. The results showed that the nanoformulations decreased the minimum inhibitory concentration (MIC) of colistin in sensitive strains while in colistin-resistant strains the MIC was not altered. However, colistin-free nanoliposomes exhibited the same antibacterial activity in sensitive and PDR strains. These results demonstrate the pharmacological potential that these polymer-decorated nanoemulsions may have to address bacterial resistance.

Keywords: colistin, nanliposomes, pandrug-resistant bacteria

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SE4-P023
DESIGN OF A MULTIFUNCTIONAL NANOSTRUCTURED SYSTEM WITH POTENTIAL APPLICATIONS IN BREAST AND CERVICAL CANCER TREATMENT

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In 2020, 19.3 million new diagnosed cases of cancer and 10 million cancer deaths were estimated worldwide. Particularly, breast and cervical cancer are the most diagnosed and major causes of cancer deaths in women. Cancer treatments include surgical tumor resection complemented by radiotherapy and/or chemotherapy, but these methods usually have limited therapeutic effects and severe side effects due to their low specificity. Alternative solutions to face these challenges include targeted therapy and thermal ablation through the use of nanoparticles (NPs) such as gold NPs with anisotropic morphologies and magnetic NPs. Because of this challenge in current cancer treatment, we have developed a nanostructured modular system with a high degree of hierarchy for the transport and release of drugs, and magneto- and photothermal treatment against cancer. The system consists of magnetic NPs (Fe_3O_4) in the core of a silica (SiO_2) shell and surrounded by multi-branched gold NPs (MBAuNPs). With each of these components, the system comprises superparamagnetic and magnetothermal behavior, hierarchical structure, and photothermal capacity. These properties were confirmed by Scanning (SEM) and Transmission Electron Microscopy (TEM), UV-Vis Spectroscopy, and the measurement of the magnetic properties using a Physical Property Measurement System (PPMS). UV-Vis spectrum showed a broad absorbance that includes the near-infrared region (NIR), which makes it possible to use the system in photothermal therapy using radiation with the same wavelength, which is harmless to healthy tissues. Also, SEM and TEM showed a core-shell system with optimal size (~150 nm) and morphology. In terms of magnetic properties, the system showed a superparamagnetic behavior, which favors its use in biomedical applications since the NPs do not retain any remanent magnetization once the magnetic field is turned off. We report the development of a multifunctional nanostructured system for local magneto- and photothermal ablation and targeted drug delivery, with potential applications in the treatment of breast and cervical cancers. This purpose was achieved by synthesizing a modular system that is constituted by a magnetic core of Fe_3O_4 NPs, a protective layer of SiO_2, and MBAuNPs. The results imply that the optical, photothermal, and magnetic properties of this system are optimal for biomedical applications.

Keywords: core-shell, multifunctional, nanotheranostic

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SE4-P024
INSULIN ENCAPSULATED IN CHITOSAN-ALGINATE NANOPARTICLES

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Diabetes mellitus, characterized by the body´s impaired regulation of blood glucose levels, presents a significant global health challenge. Despite insulin therapy being a fundamental basis in diabetes management, its effectiveness is often hindered by issues such as poor stability and rapid degradation within the body. In response to these challenges, the encapsulation of insulin within nanoparticles has emerged as a promising strategy. This approach, owing to its potential to enhance stability, regulate release kinetics, and improve drug bioavailability, holds promise for reducing dosing frequency and enhancing the efficacy of diabetes mellitus treatment.
This study focuses on the nanoencapsulation of insulin utilizing alginate and chitosan, resulting in freeze-dried nanoparticles characterized through an array of techniques including UV-VIS spectroscopy, Fourier-transform infrared spectroscopy (FTIR), Raman spectroscopy, Dynamic Light Scattering (DLS) and Atomic Force Microscopy (AFM). The AFM results indicate an average particle size of 70 nm, and the encapsulation efficiency of insulin was monitored using UV-VIS spectroscopy. Experimental findings illustrate the successful encapsulation of insulin.

Keywords: Insulin, Encapsulated, Nanoparticles

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SE4-P025
DRUG DELIVERY SYSTEM BASED LECTINS-FUNCTIONALIZED MESOPOROUS SILICA NANOPARTICLES WITH RECOGNITION TOWARDS CAMPYLOBACTER JEJUNI GLYCOSTRUCTURES

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Campylobacter jejuni (C. jejuni) is one of the most common causes reported of human gastroenteritis and it is also related to the development of Guillain-Barré syndrome. Currently, the innovative strategies to combat bacterial infections, including C. jejuni, has become a priority. The use of micro- and nanoparticles has had a notable increase in research for the development of antimicrobial agents, mainly in drug transport and release systems. The results have been growing interest in the use of nanoparticles to deliver drugs. In this work, the synthesis of drug delivery systems is proposed using lectin-modified silica particles with specific biorecognition to C. jejuni, and target the treatment towards this particular pathogen. Mesoporous silica particles modified with the lectin Maackia amurensis (Mka) and Ricinus communis (RCA) were synthesized, which were physicochemically characterized by determining particle size and morphology using atomic force

microscopy (AFM), infrared spectroscopy (FTIR) and biorecognition assays with the bacteria C. jejuni. The main results were the obtaining of particles with an average size of 5 µm, with apparent spherical morphology. Using Infrared spectroscopy, the functionalization of the particles with lectins was observed. Likewise, biorecognition assays indicate that lectin-mesoporous silica particles can bind specifically to C. jejuni, which is why they present potential applications as a targeted drug delivery system for microbial agents.

Keywords: Campylobacter jejuni, Drug delivery, Silica nanoparticles

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SE4-P027
LIPOSOMES AND GOLD NANOPARTICLES AS CARRIERS FOR INDOCYANINE GREEN AND ITS POTENTIAL USE IN PHOTODYNAMIC THERAPY

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Photosensitizers (PSs) are molecules used in photodynamic therapy (PDT) to induce the death of targeted cells by oxidative stress [1-3]. In PDT, the PS is put inside the cells. Reactive oxygen species (ROS) are produced when the PS is irradiated with a specific wavelength laser and such ROS start oxidative reactions that lead to cellular death. Indocyanine green (IG) is a molecule used in surgery and Diagnostic Imaging because its photoactive properties and because is easily excreted [4, 5]. In this work, IG was tested as photosensitizer (PS) to provoke the death of Paramecium tetraurelia (PT) under laser irradiation of 800 nm. IG was put in contact with the PT culture by four ways: directly in solution, adsorbed on Au nanoparticles (IGAuNP), encapsulated in liposomes (IGL) and IGAuNP encapsulated in liposomes (IGAuNPL). After 40 h of irradiation, PT that were in contact with IG in solution and with IGAuNPL showed 0 % survival, PT that were in contact with IGL showed 86 % survival and PT that were in contact with IGAuNP showed 96 % survival. PT that were in contact with liposomes and gold nanoparticles but without IG as it as PT that were in contact with all materials but without irradiation, showed 98 to100 % survival. This results showed several clue aspetcs: The proposed materials ans systems are innocuous if are not iiradiated; IG could be used as PS since is able to provoke the death cell after being irradiated with 800 nm light; Au nanoparticles showed a synergistic effect with IG due to its thermal photoactivity that accelerate the photoactivation of IG, although this system is not effective unless being encapsulated in liposomes. Finally, liposomes are suitable nanocarriers for the PS and Au nanoparticles given its biocompatibility which could help to achieve the targeted cells, get into them and retard the excretion from body time enough to perform PDT.

Keywords: Photodynamic therapy, Liposomal nanocarriers, Indocyanine green and Au Nanoparticles

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SE4-P028
SYNTHESIS OF NANOMOLECULES CONJUGATED WITH MEFENAMIC-TEMOZOLOMIDE ACIDS FOR

TARGETED DRUG DELIVERY

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Amino acids Janus dendrimers are less toxic and more biocompatible and biodegradable, being ideal for medical applications. In addition, bioactive dendrimer conjugates have so far been studied for their versatile capabilities to enhance stability, solubility. Janus dendrimers are a new class of dendrimers formed of two different dendrons, taking advantage of the properties of both sides. Herein, we report the synthesis of a Janus dendrimer with two different functionalities: One dendron with L-lysine-GABA conjugated with mefenamic acid as terminal group and carboxylic acid as a focal group and the second dendron with methyl acrylate-Lysine and temozolomide as terminal group and with trietylene glycol as a focal group. The Janus dendrimer was obtained via esterification reaction. Dendrons and Janus dendrimer were full characterized by NMR one and two dimensions. The anticancer activity of the mefenamic-temozolomide-conjugate showed significant cytotoxic effect against human prostatic adenocarcinoma PC-3. Moreover, the Janus dendrimer conjugate with mefenamic-temozolomide improved cytotoxicity compared to free mefenamic and temozolomide acids.

Keywords: Janus dendrimer, Mefenamic acid, Temozolomide

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SE4-P029
QUANTUM-MECHANICAL ANALYSIS OF THE gp120 GLYCOPROTEIN OF THE OUTER ENVELOPE OF WILD-TYPE HIV-1 NECESSARY TO UNDERSTAND INFECTION IN AIDS, USEFUL FOR THE DEVELOPMENT OF NEW PHARMACOLOGICAL AND THERAPEUTIC STRATEGIES

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We model the binding domain of the gp120 glycoprotein (BDgp) of HIV-1 (human immunodeficiency virus) located within the region of amino acids 365 to 430 in accordance with recent research reports, where it is stated that the entry of HIV to human cells requires the interaction of the glycoprotein of the virus´s outer envelope, gp120, with the human glycoprotein CD4 (cluster of differentiation 4). The research strategy was the analysis of BDgp using density functional theory (DFT), we identified zones of maximum reactivity, physicochemical properties and HOMO-LUMO frontier molecular orbitals useful for understanding the infection and development of the AIDS disease (acquired immunodeficiency syndrome). We also identify the most reactive biopolymers or specific amino acids susceptible to modification of gp120, necessary for the design of new pharmacological, therapeutic and prophylactic strategies.

Keywords: gp120/HIV-1, DFT THEORY, AIDS

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SE4-P030
QUANTUM-MECHANIC STUDY OF PROTEIN E OF SARS-CoV-2 AS A NEW POTENTIAL CANDIDATE IN THERAPEUTIC DEVELOPMENT TO COMBAT PROLONGED-COVID-19

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We constructed a quantum model of the short hydrophilic N-terminal domain (NTD) of the E (Envelope) protein of the wild-type SARS-CoV-2 virus essential for its pathogenesis. Based on density functional theory (DFT), we identify zones of maximum reactivity, physicochemical properties and their HOMO-LUMO frontier molecular orbitals, in addition to the most reactive sites susceptible to modification of the NTD useful for therapeutic intervention or vaccine development. The research strategy of this work was through the electronic interactions and transitions at the quantum level of the atoms that constitute NTD. Recent research reports the high mutation that the receptor binding domain (RBD) of the Spike protein of the SARS-CoV-2 virus presents, generating new variants of the virus of concern that evade detection or decrease therapeutic or vaccination efficiency in addition to a type of long-COVID, damaging various organs such as the brain, contributing to diseases such as Alzheimer´s and Parkinson´s. Our results are very useful for the development of more effective and specific treatments for this persistent form of COVID-19 by including the NTD of protein E as a therapeutic target.

Keywords: PROTEIN E (NTD) SARS-CoV-2, DFT THEORY/ PROLONGED COVID-19, ALZHEIMER´S/PARKINSON´S

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SE4-P031
COMPARATIVE QUANTUM-MECHANICAL CHARACTERIZATION OF THE MOLECULES ACACETIN AND CURCUMIN TO IMPROVE THEIR ANTIOXIDANT, ANTI-INFLAMMATORY, ANTICANCER AND NEUROPROTECTIVE FUNCTIONS

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We present results based on the density-functional Theory (DFT), that allow the comparison of their structural characteristics and sites of potential reactivity of stable structures of the molecules acacetin (4´-methoxy-5,7-dihydroxyflavone) and curcumin ((1E, 6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), in addition to the physicochemical properties and its HOMO-LUMO frontier molecular orbitals, the distribution of electric charges and the Mulliken population to determine areas and sites with excess or deficit of electrons. Recent research reports that patients who present brain inflammation caused by viruses such as SARS-CoV-2 (long COVID-19) and HIV induce an immune response that promotes mental confusion (problems with memory, concentration and decision making) and related to diseases such as Alzheimer´s and Parkinson´s. There are clinical research

reports that propose acacetin and curcumin in the prophylaxis and therapy of breast and colorectal cancer. Our results will be very useful to design and synthesize analogues with improvements in their pharmacological properties, such as greater potency, selectivity or bioavailability for therapeutic applications in their antioxidant, anti-inflammatory, anticancer and neuroprotective functions.

Keywords: ACACETIN/CURCUMIN, DFT THEORY, COVID-19/CANCER

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SE4-P032
THE ROLE OF ANTIBACTERIAL MOFs NANOSTRUCTURES IN THE FORMULATION OF HOLLOW-FIBER MEMBRANES WITH POTENTIAL APPLICATION IN HEMODIALYSIS

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Chronic kidney failure (CKD) is one of the most significant conditions worldwide since around 10% of the world´s population suffers from it. Developing polymeric nanomaterials formulated with organometallic structures has set the standard for obtaining antibacterial and biocompatible materials capable of offering viable selective separation processes in hemodialysis treatments. The present work describes the synthesis of metal-organic frameworks (MOFs) based on copper and their surface modification with SO_3 groups, with the aim of making their interaction compatible with a polyphenyl sulfone (PPSU) matrix. The results demonstrate that the combined solvothermal synthesis allows the obtaining of MOFs decorated with SO3, where the incorporation of the functional group modifies the crystalline structure of the material, which is appreciated through structural analysis using SEM, where the MOFs have particle sizes between 1 nm a 10 µm. The changes in the surface area of the MOFs due to the chemical modification demonstrate that the area decreases to 46.89 m^2/g with the incorporation of the functional group, which is directly related to the bactericidal effect of the material upon contact with S. aureus. The MOFs-SO_3 were incorporated into a hollow fiber membrane system through phase inversion, where the characteristic morphology of the double layer was corroborated by SEM. Finally, the flow analysis of the membranes formulated with MOFs demonstrates that the incorporation of the nanostructures promotes the volumetric flow of the aqueous model. As a result, the combination of the intrinsic properties of the nanocomposite represents a viable alternative for the manufacture of membranes with possible application in hemodialysis processes.

Keywords: MOFs, hollow-fiber, antibacterial

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SE4-P033
TUNING THE OPTICAL AND STRUCTURAL PROPERTIES OF YVO_4: Er, Yb UPCONVERSION NANOPARTICLES USING SYNTHESIS METHODOLOGY

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Upconversion nanoparticles (UCNP) are photoluminescent inorganic nanoparticles that can be excited using near-infrared light sources. UCNPs have been studied in electronics to form part of solar cells or in bioapplications for monitoring biomolecules and other substances [1].

To extend the applications of UCNPs at the nanoscale, the specific combination of materials, synthesis methods, size, and shape of the UCNPs must be studied to tune their luminescent properties according to the desired application.

In this study, we examined various synthesis parameters to enhance the photoluminescent intensity of YVO_4: Er, Yb UCNPs. Factors of the synthesis methodology such as co-dopant concentration, heat treatment, and cleaning process are investigated to enhance their optical characteristics. We used characterization techniques such as XRD, UV-vis, Raman, PL, and HRTEM to understand the changes in the structure and photoluminescent behaviors of YVO_4: Er,Yb UCNP. We showed that a heat treatment at 1000°C is crucial for creating upconversion energy transfer mechanisms with an optimal stoichiometric condition of $Y_{0.79}Er_{0.01}Yb_{0.2}VO_4$ for the green emission. Color properties strongly rely on the applied heat treatment and excitation source rather than the cleaning process or synthesis methodology. However, the last two affect the morphological properties of UCNPs to a greater extent.

This work allowed us to determine an optimal methodology for obtaining YVO_4: Er, Yb UCNPs of high photoluminescent intensity. Our particular focus lies in advancing the development of biosensors in bioimaging for promptly diagnosis of diseases.

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Keywords: Upconversion Nanoparticles, Bioimaging, Luminescence

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SE4-P034
MINIATURIZED ELECTROCHEMICAL IMMUNOSENSOR FOR NON-SMALL CELL LUNG CANCER BIOMARKER DETECTION

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Lung cancer (LC) is top-ranked in incidence and mortality among all types of cancer globally, and non-small cell lung cancer (NSCLC) corresponds to 85% of all LC types. It holds a 5-year survival rate of only 28% for all combined stages, in part due to the lack of technologies to diagnose the disease in an early stage, which has proven to increase patients´ survival rate. CYFRA 21-1 is a NSCLC biomarker whose content in the patient´s serum is highly related to the stage of the disease, even in the early stages. However, its low concentration in the range of nanograms per milliliter makes it hard to detect. In this work, an immunosensor using two different epitope-specific antibodies for CYFRA 21-1 detection was developed based on a gold-carbon (Au-C)

bonding strategy for antibody immobilization, which confers high conductance and stability, using a miniaturized, portable, and low-cost standard gold nanoparticle surface screen-printed electrode for the detection of the NSCLC biomarker. The developed device was tested by differential pulse voltammetry over a working range of 10^{-10} to 1 ng/mL, and highly linear models were obtained to quantify CYFRA 21-1 concentration with a limit of detection of 4.6×10^{-10} ng/mL. The developed sensor presents an unprecedented LOD and works within a wide linear range selectively detecting CYFRA 21-1. This work showcases a cost-effective technology for the early diagnosis of NSCLC with the potential to become a widely accessible point-of-care (POC) device.

Keywords: Electrochemical Immunosensor, Screen-Printed Electrode, Biomarker Detection

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SE4-P035
CHARACTERIZATION OF g-ORYZANOL NANOCAPSULES, KINETIC, AND RELEASE MECHANISM IN DIFFERENT FOOD SIMULANTS AT 25 °C

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The aim was to characterize and analyze the kinetics and release mechanism of g-oryzanol in zein-gum Arabic nanocapsules obtained by nanoprecipitation for its potential application in foods or pharmacy. The "in vitro" release kinetics were carried out at 25°C in a 0.2 M phosphate buffer solution at pH 5.5, with food simulants (10% ethanol, and 50% ethanol) with a cellulose acetate membrane per 48 h. Kinetic and empirical mathematical models (zero, first order, Higuchi and Korsmeyer, and Peppas) were considered, and diffusion coefficients were calculated. The nanocapsules with g-oryzanol had a particle size of 476 ± 24.7 nm, polydispersity index of 0.401 ± 0.06, zeta potential of -25.5 ± 0.6 mV, and encapsulation efficiency of 70 ± 0.8 %. The antioxidant capacity was 1099.55 ± 6.5 µM equivalents of Trolox, and the % radical inhibition was 88.09 ± 1.54 %. The micrography showed a spherical shape with aggregates. The kinetic model that best fits the R2 values was the zero-order model (with 2 simulants), representing that the increase or reduction of the concentration does not accelerate or slow down the diffusion. The parameters to explain the diffusion mechanism, with 10% ethanol and 50% ethanol, have values between $0.5 < n < 1$, presenting a non-Fickian (Anomalous) time-dependent transport. There is no statistical significance in diffusion coefficient, between the two simulants. Concluding that with the release kinetics and properties of the nanocapsules zein-gum Arabic with g-oryzanol obtained have the potential for use in foods or pharmacy

Keywords: Nanocapsules, Diffusion coefficient, Release kinetics

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SE4-P038
EFFECT OF GELATIN TYPE ON IN VITRO RELEASE KINETICS OF NANOENCAPSULATED THYMOL

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This research aims to understand the effect of the variation of gelatin type (A and B) used in polymeric mixture with chitosan for a nanoparticle (NP) formation to serve as a modified release system of encapsulated thymol. Both NP, formed by the emulsion-coacervation method, exhibited significant differences ($p \leq 0.05$) during their characterization, the nanoparticles-gelatin A (NP-A) presenting a particle size of 316.5 ± 2 nm, and the nanoparticles-gelatin B (NP-B) 383.9 ± 17; a polydispersity index 0.200±0.015 and 0.221±0.019, and thymol encapsulation efficiency of 88.0±3% and 83.67±5% respectively. In vitro release kinetics were carried out at 25°C in a 0.2 M phosphate buffer solution at pH 5.5 and 7.0, with a cellulose acetate membrane per 48 h. The release kinetic analysis considered mathematical models (zero, first order, Higuchi, and Korsmeyer-Peppas). NP-B presented the highest amount of released thymol ($p \leq 0.05$) at both pH conditions, related to the greater physical instability presented by the structure and lower zeta potential (ξ), demonstrated by the particle size variation over a week, NP-A (ξ =25.2 ± 1.5 mV) presented an increase ≤ 5 nm, versus a higher variation of GB-NP ≥ 20 nm (ξ=20.2 ± 2.2 mV). It also was found that for all NP, the Higuchi model ($Mt/M\infty = k\, t1/2$) is the one that most closely adhered to the behavior presented experimentally (R2=0.9900±0.0036). For the Korsmeyer-Peppas model, the “n” value was in the range of ($0.5 \leq n \leq 1$), describing a non-Fickian behavior related to the diffusion of the active compound into the medium with simultaneous viscoelastic relaxation of the polymer structure induced by the swelling of the hydrogel structure formed by polysaccharide-protein interactions. The calculated diffusion coefficients for NP-A (3.70 x10-9 m2/s) presented no effect ($p \geq 0.05$) for pH variation however, there was a difference ($p \leq 0.05$) when both types of gelatins were compared, presenting a higher value (6.71 x10-9 m2/s) in NP-B at pH 7.0. These results suggest that NP-A is most suitable to serve as a modified release profile for thymol (pH 5.5-7.0).

Keywords: Release Kinetics, Nanoparticles, Gelatin

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SE4-P039
PHOTOLUMINESCENT AND PHOTOTHERMAL EFFECT OF Fe_3O_4@ ZrO_2: Yb^{3+}-Er^{3+} FOR DIAGNOSIS AND THERAPY.

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Fe_3O_4@ZrO_2 (core@shel) nanoparticles were synthesized by a two-phase synthesis process. First, the

magnetic core (Fe_3O_4) was obtained by the thermal decomposition method [1], while the shell (ZrO_2: Yb^{3+}-Er^{3+}) was deposited on the core by the modified Stöber method [2]. Core particles of between 4 to 16 nm were obtained, when the shell was deposited the nanoparticles reached a size of 20 to 60 nm. The XRD characterizations confirm the presence of the crystalline phases of the Fe_3O_4 nucleus and ZrO_2 on the surface. As well as the presence of the functional groups of both the core and the shell were identified by FTIR.

Strong magnetic properties were observed in particles suspended in polar solvents. As well as upconversion emission from UV to IR, under 975 nm excitation, the highest emission was obtained with 14 mmol of ZrO_2: Yb^{3+}-Er^{3+}.An effective photothermal response was observed upon 3 min of laser irradiation, reaching temperatures in the range between 55 - 99 °C. Based on these results, it is expected that those nanoparticles could be used as a contrast agents for optical imaging with dual photoluminescent and magnetic responses, as well as for hyperthermia applications.

Keywords: core@shell, photoluminescence, photothermal

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SE4-P041
THE ALTERATIONS IN THE OPTICAL CHARACTERISTICS OF LIPOSOMES CONTAINING NANODIAMONDS AND PHARMACEUTICALS

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The use of liposomes to encapsulate nanodiamonds and drugs represents a valuable tool for diagnosing and treating various diseases, including cancer, which has seen a rising prevalence. By optimizing this approach, we aim to enhance its effectiveness specifically for cancer treatment.
Liposome preparation involved the use of soybean lecithin as a base, while the incorporation of nanodiamonds and drugs within the liposomes presents an opportunity to leverage their unique optical properties. This results in the development of a theranostic tool capable of transporting both drugs and a fluorescent marker.
The characterization of nanodiamonds and drugs within the liposomes has revealed alterations in their optical properties through photoluminescence (Ph), ultraviolet-visible spectroscopy (UV-VIS), and Fourier transform infrared spectroscopy (FTIR) analyses.
Utilizing fluorescent nanodiamonds offers the advantage of obtaining molecular images of tumor cells, while simultaneously enhancing drug bioavailability through their encapsulation, enabling the labeling of cancer cells and controlled drug release. These advancements contribute to reducing the toxicity and side effects associated with conventional treatments for patients.

Keywords: nanodiamonds, marker., pharmaceuticals

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SE4-P042
THERMO- AND pH-SENSITIVE POLYMERIC MICELLES CONTAINING SALICYLIC ACID AS A PRODRUG

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The development of new drug carrier systems has generated great interest due to the excessive use of drugs, enhancing side effects and generating significant pollution in wastewater. In this work, the main objective is to develop a new drug-carrying nanosystem that responds to changes in temperature and pH. Polymeric micelles present a great challenge in research, mainly due to the complexity of reaching nanometric sizes with good distribution. One of the techniques used to obtain polymers with an acceptable molecular weight distribution is reversible addition-fragmentation chain transfer (RAFT) polymerization. Previously, RAFT homopolymerization studies of oligoethylene glycol methyl ether methacrylates (OEGMA) have been reported, generating biocompatible polymers with a temperature response dependent on the molecular weight of the oligomer and the polymer. On the other hand, salicylic acid and its derivatives are well known for their biological activity, so it is not surprising that it is used to develop prodrugs, linking salicylic acid to polymers with potential pharmacological and biomedical applications. Therefore, the block copolymerization of hydrophilic segments derived from the random copolymerization of two different OEGMAs, with hydrophobic segments derived from the random copolymerization of butyl methacrylate and 2-methacryloyloxy benzoic acid, was studied. The obtaining of these copolymers was carried out using the RAFT technique with which it was possible to establish the most efficient conditions for the synthesis, which was followed by Nuclear Magnetic Resonance and Gel Permeation Chromatography analysis, which confirmed the successful obtaining of copolymers of controlled molecular weight; Furthermore, the self-aggregation and thermo- and pH-sensitive response were confirmed by dynamic light scattering analysis, fluorescence spectroscopy, and scanning electron microscopy. The obtaining of micellar aggregates of sizes between 40-100 nm sensitive to pH changes, and with a thermosensitive response between 35 and 40 °C, showing potential for the loading and release of drugs, in conjunction with salicylic acid, was confirmed.

Keywords: Smart-polymers, Block copolymers, Self-Assembly

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SE4-O019
ENHANCING ANTIOXIDANT PROPERTIES OF CERIUM OXIDE NANOPARTICLES THROUGH NEODYMIUM DOPING FOR BIOMEDICAL APPLICATIONS

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Rare earth nanoparticles (NPs) are used in biotechnological and biomedical applications. In this study, CeO_2 NPs doped with ceria and neodymium (Nd^{3+}) were prepared by chemical methods. The effect of Nd^{3+} incorporation on the size, structure, and surface charge of CeO_2NPs (CN0, CN1, CN5, and C10) was analyzed using microscopic and mechanical methods. Antibacterial activity was evaluated against Gram-positive and Gram-negative bacteria. Cytotoxicity was studied using breast cancer cell lines and antioxidant activity was tested using DPPH and ABTS assays. The results exhibited that the CeO_2NPs were spherical and showed an average size of 10.23 nm, while the incorporation of Nd^{3+} raised the presence of 18.87 nm nanorods. However, no antibacterial or anticancer activity was found. It was found that the samples CN0, CN1, and CN5 were good antioxidants because they inhibited the formation of DPPH and ABTS free radicals with IC_{50} values ranging from 28 to 190 µg/mL. CN10 presented IC50 values of 18.93 and 47.73 µg/ml in both assays, considered a higher antioxidant. Considering the obtained results, CeO_2-NPs can be explored for future applications in biomedical fields.

Keywords: CeO2, Antioxidat, Machine learning

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SE4-O020
THE CYTOTOXIC EFFECT OF DISULFIRAM-LOADED POLY-ε-CAPROLACTONE NANOPARTICLES IN ADIPOSE TISSUE CELLS: IN VITRO ASSESSMENT

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Novel treatment strategies are being developed against obesity. Disulfiram (DSF) has been proposed as an alternative treatment to metabolic disorders, including obesity, however it is of low bioavailability due to high instability under physiological conditions, limiting its clinical application. Here, we optimized the synthesis and characterized poly-ε-caprolactone (PCL) nanoparticles (NPs) loaded with DSF, also we analyzed the cytotoxicity on adipose cells. NPs were synthesized by nanoprecipitation method, varying its solvent, either acetone or acetone/dichloromethane (60:40) (v:v), and proportion PCL:DSF (w:w) 1:2, 1:1, 2:1 and, 1:0. The cell viability was assessed by alamar blue assay, mitochondrial reactive oxygen species (mROS) production and phosphatidylserine exposure by flow cytometry and finally clonogenicity by crystal violet stain. The best condition was obtained in the ratio 2:1 PCL:DSF and acetone/dichloromethane solvent mixture. NPs were spherical with a particle size distribution of 203.2 ± 29.33 nm, a PDI of 0.296 ± 0.084, a ζ-potential of -20.7 ± 4.58 mV, and a physical drug loading of 8.6 ± 5.80 %. A sustained release was observed from 0.5 h up to 96 h under physiological conditions. Then, we determine in vitro cytotoxicity of NPs on adipose cells including preadipocytes, white-like adipocytes, and macrophages assessing cell viability, mROS production and cell death. Here, we demonstrated for the first time the cytotoxicity of encapsulated DSF into PCL NPs on adipose cells in vitro. PCL-DSF NPs did not modify cell viability on white-like adipocytes and macrophages. In preadipocytes the NPs decrease cell viability inversely proportional to concentration, also induces mROS production augmentation, leading to regulated cell death. Finally, long-term proliferation inhibition was observed. This data suggest the bioequivalent effect of PCL-DSF NPs compared to free DSF. Our findings, suggest a novel strategy for DSF long-term delivery to obesity treatments.

Keywords: Adipose tissue, Disulfiram, Drug delivery

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SE4-O022
EVALUATION OF IMMUNE RESPONSE INDUCED BY FUNCTIONALIZED MESOPOROUS SILICA PARTICLES AS CARRIERS OF PLASMIDS THAT CODIFY FOR FUSION PROTEINS OF SARS-COV-2.

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The next generation of COVID-19 vaccines has focused on using more than one SARS-CoV-2 antigen to induce a long-lasting immune response. Although mRNA SARS-CoV-2 vaccines have been shown efficacy, safety, and security, DNA vaccines against several viruses have exhibited higher stability and longer storage time. The micro and nanomaterials as carriers and/or adjuvants have shown improvements over antigens, regarding the stability and immune response. In the present work, we design two plasmids that codify for fusion proteins with the most immunogenic regions of S and N protein of SARS CoV-2 delta (D-S1N) and omicron (O-SN) strains. Sequences of fusion proteins were cloned into eukaryotic expression vector pcDNA3.1. Thus, we synthesized silica mesoporous particles (MSP) (~ 1800 nm, -10 mV) functionalized with APTES, and performed interactions with the plasmids pcDNA3.1/D-S1N and pcDNA3.1/O-SN. After coupling between MSP and DNA, we performed in vitro and in vivo assays. BALB /c mice were immunized with 25µg of pcDNA3.1/D-S1N, pcDNA3.1/O-SN, or pcDNA3.1 coupled or not to MSP. Three immunizations with intervals of 20 days were performed before each immunization mice were bled, and serum samples were obtained. Mice immunized with pcDNA3.1 or just MSP were used as controls Specific antibody responses of IgM and IgG against the N, S1 proteins were determined. We determine the cito-toxicity of our MSP by in vitro assays. We evaluated different rates of DNA: MSP and obtained a percentage of coupled since 20 to 90% for both plasmids. After the immunization scheme, antibodies against S1 and N were determined in mice immunized with pcDNA3.1/D-S1N and pcDNA3.1/O-SN.

Keywords: Silica Mesoporous Nanoparticles, DNA Vaccines, SARS-CoV-2

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SE4-O023
VECTORIZED HALLOYSITE NANOTUBES WITH PEG-FOLIC ACID AS DRUG DELIVERY CARRIER FOR DOXORUBICIN

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Halloysite nanotubes (HNTs) are natural nanosized tubular clay minerals with potential application in biomedicine as drug delivery system. In this study, HNTs was modified with poly-[ethylene glycol]-folic acid of 1000 Da (PEG-FOL) to produce vectorized nanocarriers for enhancement in cancer chemotherapy. The nanocarrier was prepared using (3-isocyan-propyl)-triethoxysilane (IPTES) as coupling agent to immobilize PEG-FA. The pristine HNT and PEGylated HNT were characterized using XRD, TEM, N_2 adsorption-desorption isotherms at -196°C, DRS UV-Vis and TGA. The nanomaterials efficiently encapsulated doxorubicin (DOX) as model antiproliferative drug. The pristine HNT and HNT-PEG-FOL carriers showed a loading efficiency of 13.2 mg/g and 4.1 mg/g for the encapsulation of DOX, respectively. The carriers showed pH-dependent release of DOX and adjust their release profile at first order kinetic model. The release at pH = 5.5 for both nanocarriers was faster than at pH = 7.4. Hemolysis assays indicated that pristine HNT was toxic - at high dosages – whereas HNT-PEG-FOL was a biocompatible nanocarrier with no toxicity for red blood cells. Additionally, Alamar Blue for HeLa and MCF7 cells viability assays reveal that both nanocarriers are not cytotoxic materials over a wide concentration range. Furthermore, the formulation of HNT-PEG-FOL:DOX showed a higher cytotoxic effect in HeLa cells compares to MCF7 cells. The results suggested that the vectorized HNT nanomaterial had great potential as a nanocarrier in target chemotherapy for the cancer cells lines that overexpress the folate receptors.

Keywords: Halloysite, Drug delivery, Biocompatible

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SE4-O024 Invited Talk
30,000 NANOTEXTURED SPINAL IMPLANTS WITH NO FAILURES…AND STILL COUNTING

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This invited presentation will highlight how to design medical devices to eliminate implant failure through the use of nanotextures. Specifically, nanotextures were implemented onto the surfaces of current spinal implants inserted into over 30,000 patients over the past 5 years. To date, none of these implants have failed: no infection, no chronic inflammation, and no implant loosening. The average implant failure rates of conventional spinal implants ranges from 5 – 10%. Fundamental studies will be given which highlight the unique surface energy provided by nanotextures that can control initial protein adsorption to in turn control cell adhesion and subsequent tissue formation. Studies will also be presented in which nanotextures are being implemented for other medical devices including vascular, wound healing, neurological and others.

Keywords: medical devices, nanotextures, spinal implants

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SE4-O025
FERRITIN-AU(I) BIOCONJUGATES AS ANTICANCER AGENTS

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Human heavy-chain ferritin (HuHf) is a recombinant protein composed of 24 H-subunits, forming a nanocage with a hollow globular structure. The H-chain is recognized by the transferrin receptor-1 (TfR1), overexpressed in many cancer cell lines. HuHf is a suitable nanocarrier due to its versatility, excellent safety profile and nano-range size[1]. Gold compounds are potential anticancers with antiproliferative and proapoptotic properties[2]. Here, I worked on the development of human heavy chain ferritin conjugates with different gold(I) compounds, i.e. Auranofin[3], Aurothiomalate and a monocarbene, for the production of ferritin-based nanocarriers and their selective delivery toward cancer cells. Five human-H chain ferritins were expressed in E. coli cells: the wild type, three different mutants, where I replaced with Alanine one or two cysteines (C130A, C90AC102A and C90A) and a ^{19}F labelled- human ferritin (5-F-Trp93). I exploited the use of recombinant wild type HuHf for the targeted delivery of the gold(I) compounds, the three mutants to determine their binding sites on the protein and the ^{19}F-labelled ferritin as a probe for cellular uptake via ^{19}F NMR studies. For all the HuHf-gold(I) adducts: ESI-MS spectrometry (measuring the disassembled subunits) confirmed the adducts formation and provided information on the chemical nature of the species present in solution. ICP determined the total amount of gold per cage. Also, biological experiments were performed to evaluate the cytotoxicity of the free drugs and their bioconjugates with ferritin against A2780 ovarian cancer cells; moreover, the cytotoxicity of the free compounds was evaluated together with the TfR1 expression in four different cell lines i.e. U87MG glioblastoma cells, MCF-7 breast cancer cells, HCT-116 colorectal cancer cells and MRC-5 fibroblast cells.

Keywords: Human heavy chain ferritin, nanocarrier, anticancer metal based drugs

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SE4-O026
DEVELOPMENT OF NANOSCALE POLYMER-BASED STRATEGIES TO TARGET ADIPOSE TISSUE

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Introduction

Recent research has identified ASC-1 (Alanine, Serine, Cysteine Transporter-1) as a surface marker for white adipocytes. Nanoscale strategies, such as nanoparticles (NPs) functionalized with homing peptides like SMLC (S-Methyl-L-Cysteine), could then be applied for targeted delivery of anti-obesogenic compounds to adipose tissue cells, such as white adipocytes. The first part of this study involves the preparation of NPs that can target white adipocytes.

Methods

For the co-polymer synthesis, PLGA-COOH (poly (lactic-co-glycolic acid with carboxyl termination) was activated using an EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) /NHS (n-hydroxy succinimide) protocol to obtain PLGA-NH_2. Then, it was functionalized with NH_2-PEG-COOH (amine carboxyl terminated

heterobifunctional polyethylene glycol).

The NPs were synthesized as an oil-in-water emulsion with a combination of co-polymer and PLGA-COOH. Briefly, the polymers dissolved in acetonitrile, and then the solution was added dropwise matter into distilled water under sonication and stirred. NPs were activated with EDC/NHS protocol to functionalize with SMLC. Samples were freeze-dried and stored.

The Dynamic Light Scattering (DLS) and ζ-potential were performed with a Malvern Zetasizer Nano ZS90. DLS data was post-processed with a CONTIN method implemented in MATLAB. The samples were analyzed by Scanning Electron Microscopy (SEM) and Elemental Quantification (EDX) with a JEOL JSM-7401F Field Emission Scanning Electron Microscope.

Results

The NPs were divided into two groups: PLGA-b-PEG and PLGA-b-PEG-SMLC. The former group showed a hydrodynamic particle size distribution of 253.88 ± 10 nm and a ζ-potential of -27.44 ± 3 mV. For the latter group, the hydrodynamic particle size distribution was 272.11 ± 6 nm with a ζ-potential of -30.51 ± 4 mV. The morphology of PLGA-b-PEG-SMLC NPs was spherical, and the presence of nitrogen was detected, which doubled its percentage in samples with a higher proportion of SMLC.

Conclusions

Changes in physicochemical parameters between PLGA-b-PEG-SMLC and PLGA-b-PEG NPs suggest a successful functionalization of SMLC. Results will be further verified by nuclear magnetic resonance structural characterization, and then cellular association/internalization studies will follow up.

Keywords: ASC-1, SMLC, Nanoparticles

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SE4-O027 Invited Talk
NANOIMMUNOMEDICINE IN CANCER THERANOSTICS

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According to National Cancer Institute reports, Cancer has become the second largest cause of death in Mexico and is responsible for 13.7% of annual mortality in the country. There were 14.1 million new cáncer cases all over the world, with 8.8 million cáncer deaths in 2015 worldwide, as per World Health Organization (WHO). The cáncer incidence and mortality is approximately 25% higher in men than in women. In men, the highest mortality is due to lung cáncer while in women, it is due to breast cáncer. (1) Breast cancer (BC) is the leading cancer killer among women aged 20–59 years worldwide one million cases of breast cancer are diagnosed annually worldwide.
Chemotherapy is ineffective and hence there is a need to have a double pronged action which includes both chemo as well as Immunotherapy. The reason behind this coupling is that tumor cells being heterogeneous are continuously evolving, and hence drugs that are supposed to kill tumor cells, select for resistant clones

leading to relapse. Whereas immune cells coordinate well, coupling both innate as well as adaptive immune response is quite impressive. Moreover, the adaptive immune response is gifted with memory, which doesn't exist in any other form of therapeutic modality. (5). There are many different kinds of anti-cancer drugs that can also contribute towards inducing apoptosis in tumor cells which can indirectly induce the Macrophages by creating chemotactic gradient formation as well as cytokine secretion. Magnetic nanoparticles are more advantageous as anti-cancer drug-delivery systems due to low localized and systemic toxicity, altered pharmacokinetics and proper biodistribution of the drugs and furthermore, they can themselves act as an adjuvant for APC activation.
Magnetic nanoparticles when coupled with anti-cancer drugs can help in targeted killing of cancer cells but due to resistance in the cancer cells, it is imperative to activate special immune cells that can help in the manipulation of the cancer cell resistance and induce cancer cell death with an aid of immune cells.

Keywords: Magnetic nanoparticles, Macrophages, anti-cancer drugs

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SE4-O028
SUGAR-BASED BIOFUNCTIONAL COATING OF IRON-OXIDE NANOPARTICLES: ULVAN OLIGOSACCHARIDES IN THERAGNOSTICS

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The development of multifunctional nanoparticles (NP) for targeted drug delivery and imaging in oncology remains challenging. Several obstacles, including clearance pathways, targeting strategies, and suitable therapeutic modes of action persist. To explore these challenges, this project proposes utilizing bioactive marine oligosaccharide (OS) coatings on extremely small iron-oxide nanoparticles (ESIONP).
This innovative OS coating is derived from marine sulfated Ulvan (ULV), a polysaccharide (PS) produced by a green algae that has largely been neglected in nanomedicine development. These sugars, which are rich in uronic acid, xylose and rhamnose saccharide residues, are known for their promising antitumor effects. They exhibit conventional antiproliferative activity and act as structural mimetics of glycosaminoglycans, offering original properties for controlling pro-tumoral pathways in the tumor microenvironment (TME). This polypharmacology is intriguing, as the TME may be more accessible to the NP than cancer cells, depending on the patient´s tumor biology. Despite these advantages, ULV-based coatings have been barely included in NP formulations. In contrast, the ESIONP core serves a dual purpose as diagnostic agents in magnetic resonance imaging (MRI) and as potential immunomodulators of tumor-associated macrophages.
Here, we present the preparation of OS ULV-coated ESIONP by a microwave approach that relies on hydrazine reduction of iron salt followed by an ultrafast thermic treatment for crystal growth in the presence of OS for in situ ESIONP stabilization. A design of experiment plan, optimized key reaction variables to meet predefined quality targets, including low hydrodynamic size, monomodal distribution, and suitable relaxometric properties for MRI contrast agent use. The best NP candidates were further characterized in terms of TEM, core crystallinity, stability, surface charge, and coating description.
Regarding the biological activity, the antiproliferative effect of NP formulations were assessed on the invasive breast triple-negative cancer using the MDA-MB-231 cell line as a model. As a model of their possible therapeutic action among the TME, their inhibitory activity against heparanase (HPSE), a key pro-tumoral

enzyme excreted in the extracellular matrix, was evaluated. Finally, preliminary MRI experiments were conducted on healthy mice to study their pharmacokinetics properties and their in vivo behaviors.

Keywords: Ulvan, Iron Oxide Nanoparticles, MRI

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SE4-O029
PORPHYRIN-BASED NANOPARTICLES TO IMPROVE PHOTODYNAMIC THERAPY

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Photodynamic therapy (PDT) is a promising anticancer noninvasive technique that relies on the generation of reactive oxygen species (ROS). Unfortunately, PDT still has many limitations including the poor water solubility of the photosensitizers, which are a key player for PDT. Nanomaterials are excellent delivery systems for the efficient codelivery of two or more therapeutic agents. In this work, we report on the use of the co-precipitation approach to fabricate nanoparticles containing porphyrin derivatives as photosensitizers. Three different types of nanoparticles were synthesized using commercially available tetraphenyl-porphyrin (TPP) and aminophenyl-triphenyl-porphyrin (ATPP); moreover, a novel porphyrin-based ligand containing polyhedral oligomeric silsesquioxane molecule (POSSP) was also utilized. The physicochemical and photophysical properties of the nanoparticles were determined using dynamic light scattering, electrophoretic mobility, scanning electron microscopy, ultraviolet-visible spectroscopy, and singlet oxygen assay. Cancer cells were used to evaluate the internalization, phototoxicity and cell death mechanism associated with the porphyrin-based nanoparticles. It was found that better photodynamic therapy performance for the nanoparticles as compared with the parent porphyrins. We envision that the promising results in the use of porphyrin-based nanomaterials against cancer pave the way of its evaluation in preclinical models.

Keywords: Porphyrin-based nanoparticles, Photodynamic therapy, Polyhedral oligomeric silsesquioxane

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SE4-O030
A NANOMATERIAL PROBE THAT CHANGES FLUORESCENCE COLOR UPON CLEAVAGE

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Fluorescence resonance energy transfer (FRET) reporters are commonly used in the final stages of nucleic acid amplification tests to indicate the presence of nucleic acid targets, where fluorescence is restored by nucleases that cleave the FRET reporters. However, the need for dual labelling and purification during manufacturing contributes to the high cost of FRET reporters. Here we demonstrate a low-cost silver nanocluster reporter that does not rely on FRET as the on/off switching mechanism, but rather on a cluster

transformation process that leads to fluorescence color change upon nuclease digestion. Notably, a 90 nm red shift in emission is observed upon reporter cleavage, a result unattainable by a simple donor-quencher FRET reporter. Electrospray ionization mass spectrometry results suggest that the stoichiometric change of the silver nanoclusters from Ag13 (in the intact DNA host) to Ag10 (in the fragments) is probably responsible for the emission color change observed after reporter digestion. Our results demonstrate that DNA-templated silver nanocluster probes can be versatile reporters for detecting nuclease activities and provide insights into the interactions between nucleases and metallo-DNA nanomaterials.

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Keywords: Non-FRET probes, Silver nanoclusters, Fluorescence sensing

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