safe nmt

CATALOGUE OF SERVICES

26.02.2021

- Size, distribution, morphology and concentration
- Surface characterisation
- Chemical composition
- Drug loading/release
- Optical characterisation
- Bio-nanointeraction studies
- Formulation development and manufacturing

NANOPARTICLES CHARACTERISATION

- Cytotoxicity
- Oxidative stress
- Genotoxicity
- Autophagy
- Cellular uptake
- Organs toxicity
- Immunology
- Stability
- Hematology

IN VITRO

- Small animal models
- Large animal models
- Models of disease

IN VIVO

- Affinity Molecules development
- Conjugation chemistries
- IVD development
- Biomarkers – discovery & monitoring
- Biofunctional consumables for IVD
- Registration of IVD

DIAGNOSTICS

- Computing
- Modelling

IN SILICO

- Biofilm antimicrobial properties
- Efficacy studies
- Registration

BIOFILMS

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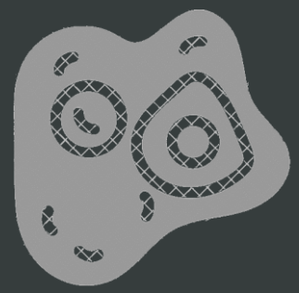
GENOTOXICITY



CELLULAR UPTAKE

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HEMATOLOGY

OXIDATIVE STRESS

AUTOPHAGY

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STERILITY

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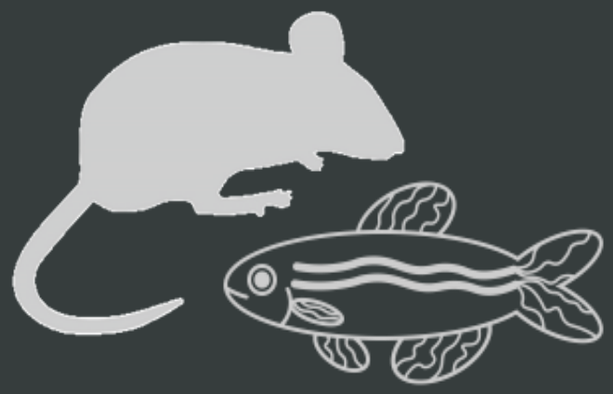
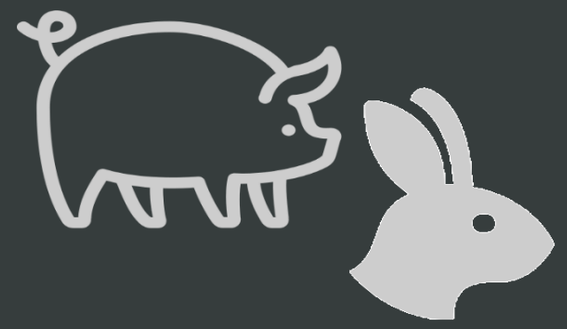
SMALL ANIMAL MODELS



MODELS OF DISEASE

ASSAYS

LARGE ANIMAL MODELS



MODELS OF DISEASE

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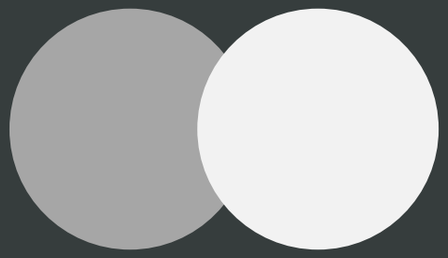

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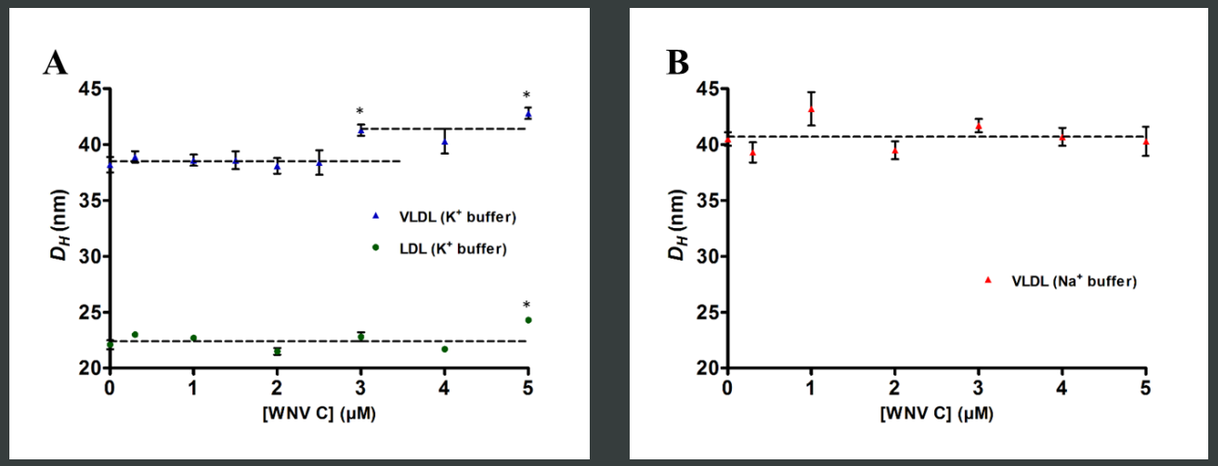
SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

DLS

Dynamic Light Scattering (DLS) measures the hydrodynamic diameter of nanoparticles in solution and provides information on the aggregation state of nanoparticles in solution. Generally NPs aggregation propensity depends on temperature, time, pH and ionic strength of the dispersant/medium. These properties need to be checked in order to predict, how NP will behave when performing *in vitro* (or *in vivo*) studies.

NTA

Nanoparticle tracking analysis (NTA) provides the hydrodynamic diameter, sized distribution, charge and particle concentration in aqueous solutions, with higher resolution than DLS. Made suitable for high-throughput analysis by addition of an autosampler.



Interaction of lipid droplets with a viral protein

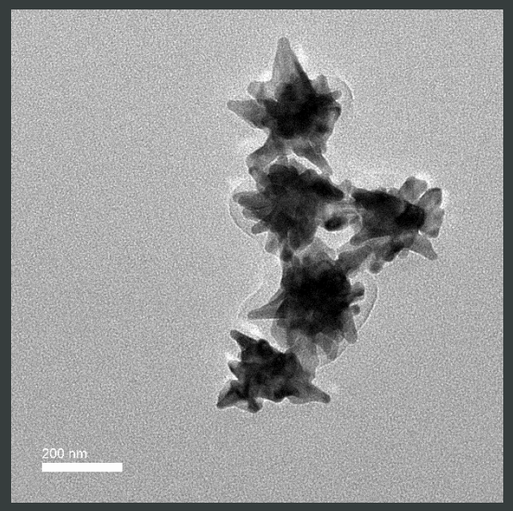
Credits: Ana Martins, Instituto de Medicina Molecular

Next

SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

TEM

Transmission Electron Microscopy (TEM) is a technique that uses an electron beam to image a nanoparticle sample, providing much higher resolution than is possible with light-based imaging techniques. TEM is the preferred method to directly measure nanoparticle morphology.



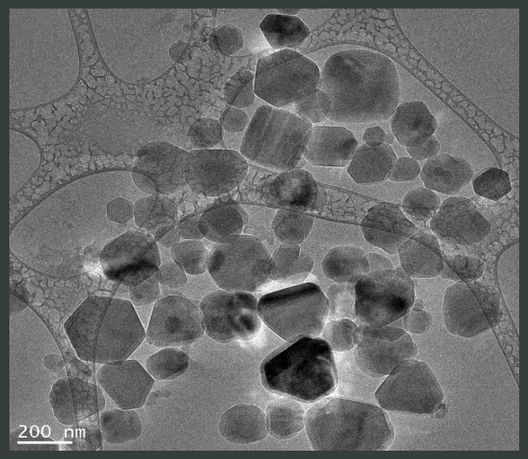
Gold nanostars

Credits: Sara Abalde-Cela, Marta Aranda, María Relvas***,***

International Iberian Nanotechnology Laboratory

Cryo-TEM

Cryogenic transmission electron microscopy (cryo-TEM) is an electron microscopy technique applied on samples cooled to cryogenic temperatures and embedded in an environment of vitreous water. The utility of transmission electron cryomicroscopy stems from the fact that it allows the observation of specimens that have not been stained or fixed in any way, showing them in their native environment.



Cubosomes

Credits: International Iberian Nanotechnology Laboratory

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SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

TEM-SAED

Selected area electron diffraction (SAED), is a crystallographic experimental technique that can be performed inside a TEM.

As a diffraction technique, utilizes an electron beam to interact with the material of interest and form a 2D image. TEM-SAED provides dry size distribution, shape, concentration, thickness and coating morphology.

XRD

X-ray diffraction (XRD) is a versatile, non-destructive technique which provides detailed information on the micro and crystallographic structure and chemical composition of all types of synthesized as well as natural materials. This method has proven to be a valuable research tool for analysing nanostructures.

MALS

Multiangle light scattering (MALS) describes a technique for measuring the light scattered by a sample into a plurality of angles. It is used for determining both the absolute molar mass and the average size of molecules in solution, by detecting how they scatter light.

VSI

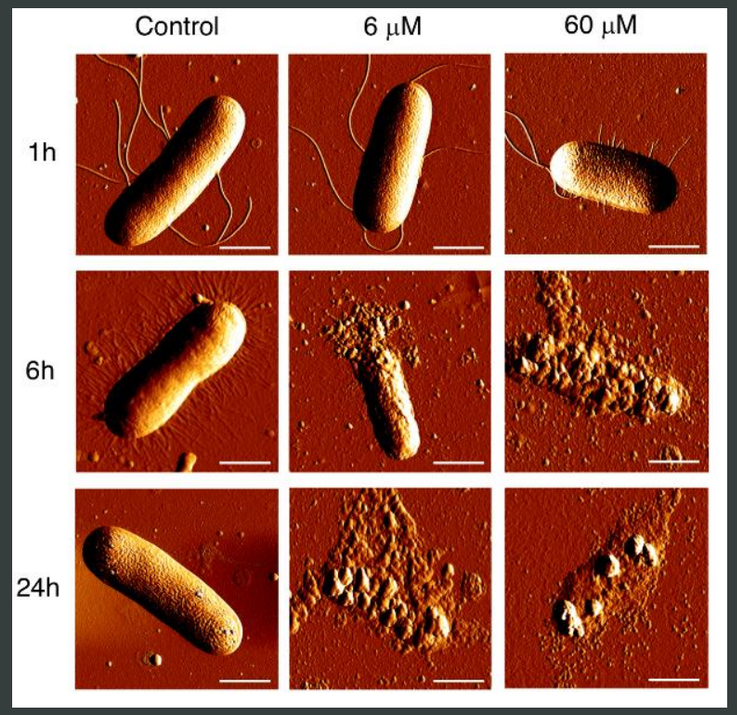
Vertical Shift Interferometry (VSI) is used for measuring features in the range of 140 nm to several µm. VSI is based on white light vertical scanning interferometry, which is a bright and dark pattern resulting from splitting a beam where one part is reflected against a reference mirror surface and the other against the sample. After reflection, the beams are recombined in the interferometer. The interferometric objective moves vertically to scan the surface at varying heights.

Next

SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

AFM

The Atomic Force Microscope (AFM) allows for 3D characterisation of nanoparticles. Unique advantages of AFM nanoparticle characterisation include the direct visualization of hydrated nanoparticles/liquid medium and the detection of specific interaction forces between molecules based on the AFM sensitivity.



Antimicrobial peptide activity in E. coli, time and concentration depending

Credits: Sónia Abreu, Instituto de Medicina Molecular

Interaction between lipid droplets/ lipoproteins and a viral protein

Credits: Ana Martins, Instituto de Medicina Molecular

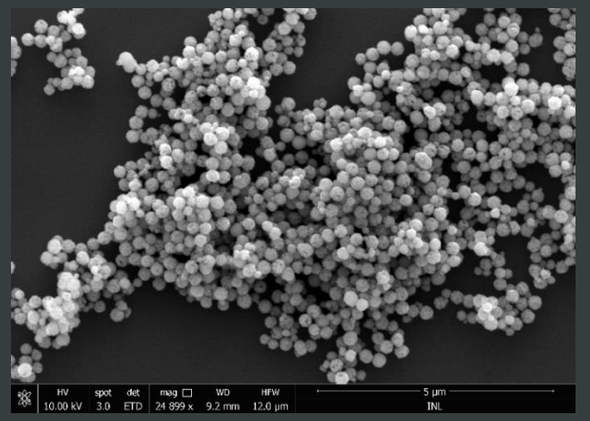
Next

SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

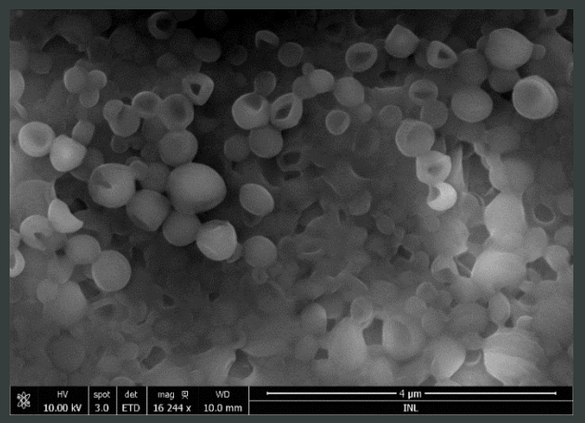
SEM and High-Resolution SEM

A scanning electron microscope (SEM) is a type of electron microscope that produces images of a sample by scanning the surface with a focused beam of electrons. The electrons interact with atoms in the sample, producing various signals that contain information about the surface topography and composition of the sample.

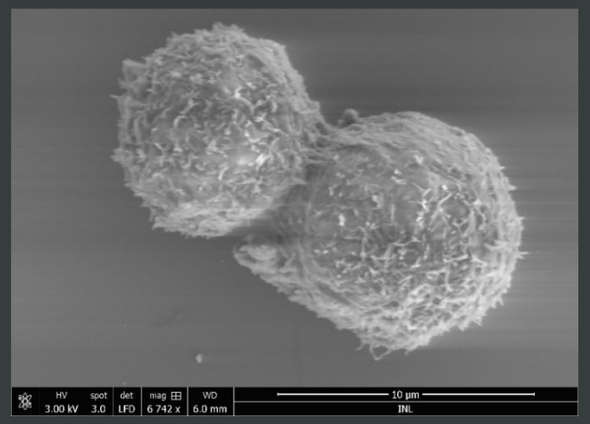
The main difference between SEM and TEM is that SEM creates an image by detecting reflected or knocked-off electrons, while TEM uses transmitted electrons (electrons that are passing through the sample) to create an image. As a result, TEM offers valuable information on the inner structure of the sample, such as crystal structure, morphology and stress state information, while SEM provides information on the sample's surface and its composition.



Magnetic NPs



Solid lipid NPs



Cells incubated with graphene-coated NPs

Credits: International Iberian Nanotechnology Laboratory

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SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

ES-DMA

Electrospray-differential mobility analysis (ES-DMA) is a powerful technique for the measurement of nanoparticle size distributions and has recently yielded promising results when measuring the absolute nanoparticles number concentrations in colloidal suspensions.

FFF-MALS

Multi-angle light scattering coupled with field-flow fractionation (FFF-MALS) creates a powerful system for accurate and robust characterisation of molar mass and size distributions for simple or complex samples.

FIB

Focused Ion Beam (FIB) is a laser imaging tool to confirm material integrity. FIB is also capable of milling controlled lines into surfaces. While the SEM uses a focused beam of electrons to image the sample in the chamber, a FIB setup uses a focused beam of ions instead.

Next

SIZE, DISTRIBUTION, CONCENTRATION AND MORPHOLOGY

FCS

Fluorescence correlation spectroscopy (FCS) is a correlation analysis of fluctuation of the fluorescence intensity. The analysis provides parameters of the physics under the fluctuations. One of the interesting applications of this is an analysis of the concentration fluctuations of fluorescent particles in solution.

CPS

Centrifugal particle sedimentation (CPS) is one of the preferred method to measure the particle size with high resolution and accuracy.

SAXS

Small-angle X-ray scattering (SAXS) is a small-angle scattering technique by which nanoscale density differences in a sample can be quantified. This means that it can determine nanoparticle size distributions, resolve the size and shape of (monodisperse) macromolecules, determine the internal structure of materials (powders and solutions), determine pore size and characteristic distances of partially ordered materials.

Menu

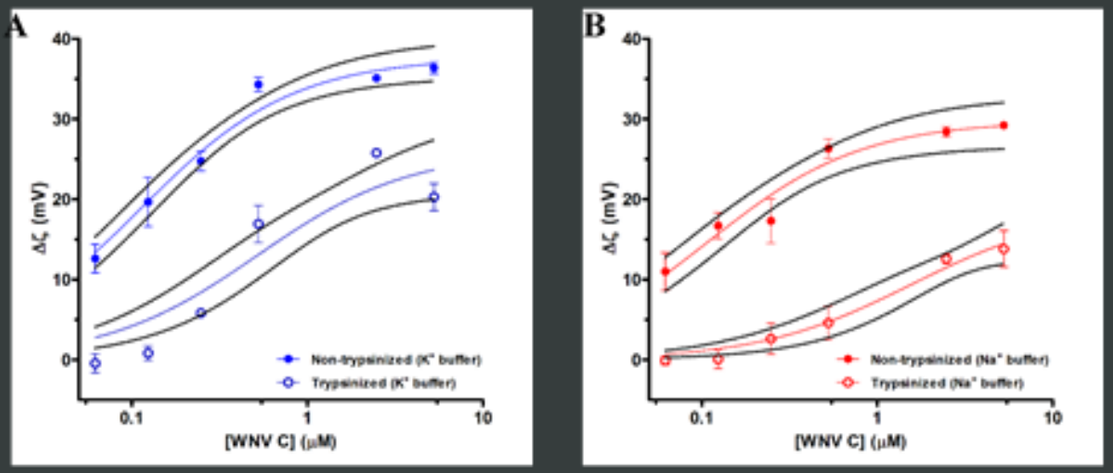
SURFACE CHARACTERISATION

Zeta Potential

Zeta potential values provide an indirect measurement of the net charge on the nanoparticle surface. Among different approaches to characterize the superficial properties of NPs in liquid state, zeta potential measurement is one of the most accessible.

Contact Angle Meter

Contact angle measurement (interfacial properties between solid/liquid system) gives remarkable data on wettability. It can also be used to analyse the processes of coating, cleaning, and surface finishing (implants or IVD, coated antimicrobial surface).



Interaction of lipid droplets with a viral protein

Credits: Ana Martins, Instituto de Medicina Molecular

PSI

Phase shifting interferometry (PSI) is a well-established technique for areal surface characterisation that relies on digitization of interference data acquired during a controlled phase shift, most often introduced by controlled mechanical oscillation of an interference objective. It allows roughness measurements. Small features (1 to 140 nm) can be measured.

Next

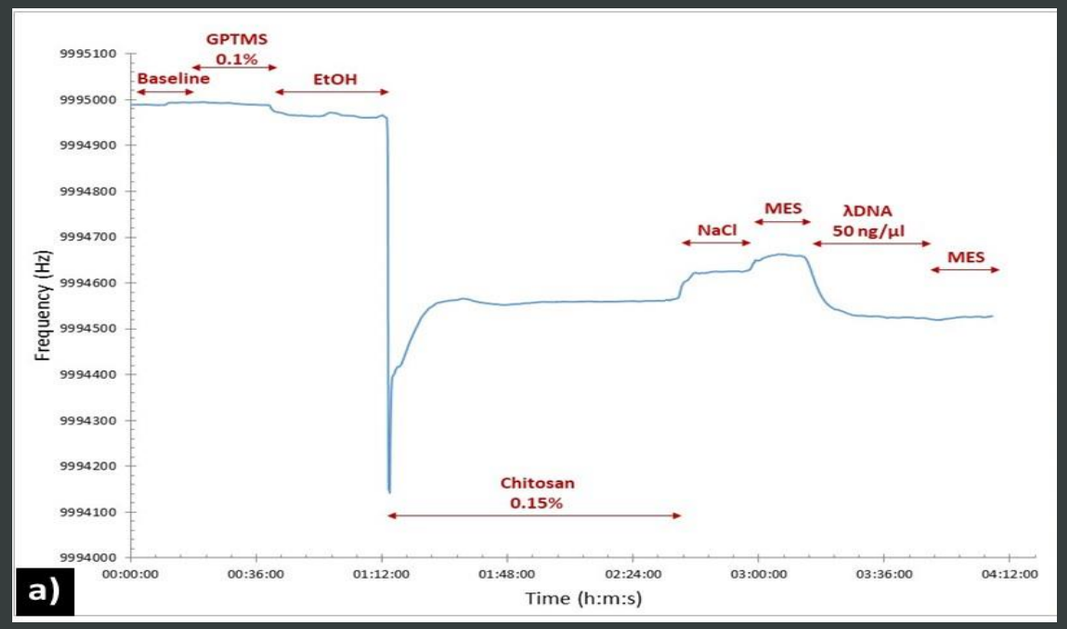
SURFACE CHARACTERISATION

QCM

Quartz Crystal Microbalance (QCM) is an extremely sensitive mass balance that measures nanogram to microgram level changes in mass per unit area. The heart of the technology is a **quartz** disc.

Profilometry

Profilometry is a technique used to extract topographical data from a surface. This can be a single point, a line scan or even a full three dimensional scan. The purpose of profilometry is to get surface morphology, step heights and surface roughness.



Measurements of system functionalisation

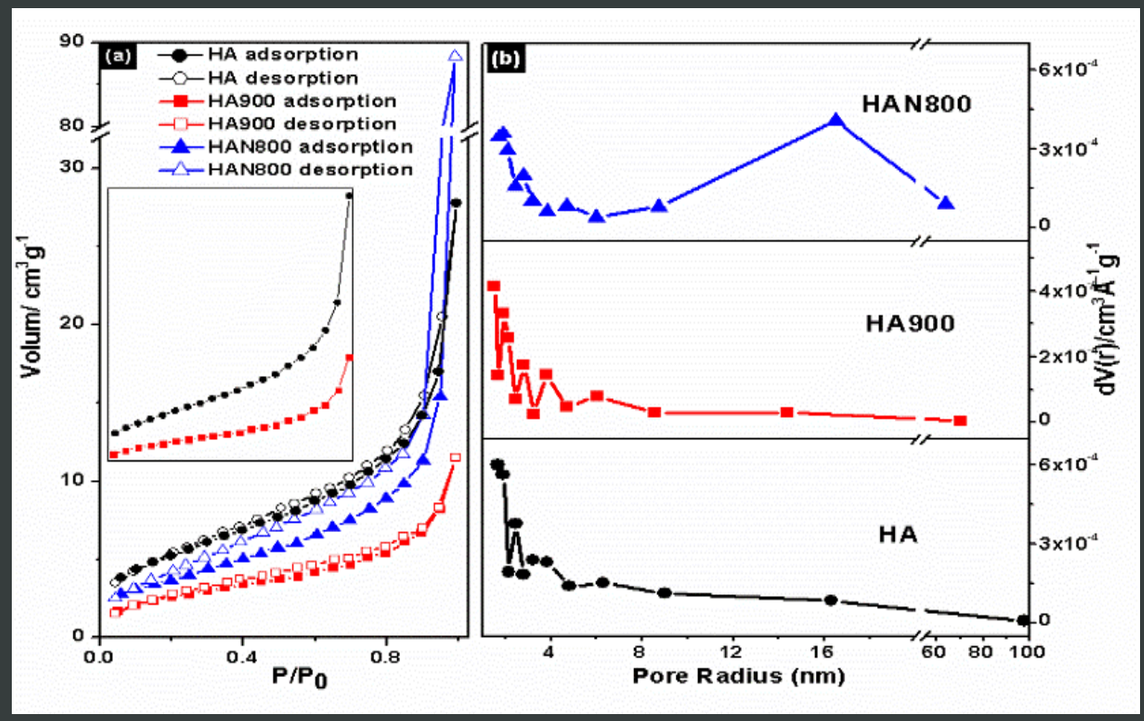
Credits: Joana Carvalho, International Iberian Nanotechnology Laboratory

Next

SURFACE CHARACTERISATION

BET

BET (Brunauer, Emmett and Teller) analysis provides precise specific surface area evaluation measured of materials, including the pore size distribution, by nitrogen adsorption measured as a function of relative pressure. This information is used to predict the dissolution rate, as this rate is proportional to the specific surface area. Thus, the surface area can be used to predict bioavailability. Further it is useful in evaluation of product performance and manufacturing consistency.



BET analysis: (a) Adsorption–desorption isotherms; (b) pore size distribution for HAP powders.

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

Next

SURFACE CHARACTERISATION

EDX

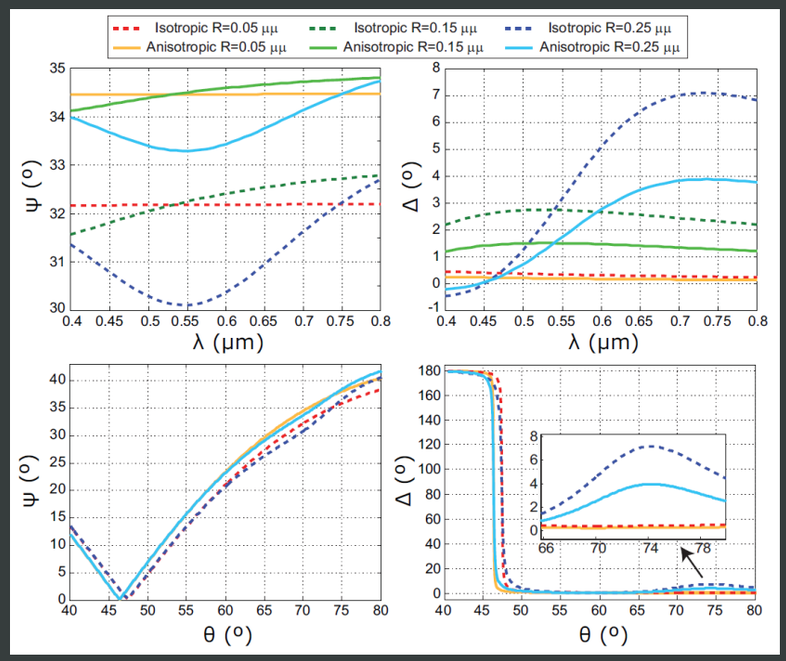
Energy-dispersive X-ray diffraction (EDX) is an analytical technique for characterizing materials. It differs from conventional X-ray diffraction by using polychromatic photons as the source and is usually operated at a fixed angle. EDX can be used to determine the crystal phase(s) in a layer or in a powder.

ToF-SIM

Surface analysis of organic and inorganic materials (mass spectrum), Map of chemical elements present in the surface of the sample, Profile analysis / sample analysis in depth.

Ellipsometry

Ellipsometry is an optical technique for investigating the dielectric properties (complex refractive index or dielectric function) of thin films. Ellipsometry measures the change of polarization upon reflection or transmission and compares it to a model. It can be used to characterize thickness of layers, and the composition, porosity and roughness of materials on a surface.



Ellipsometry measurements of liposomes above a lipid bilayer

Credits: International Iberian Nanotechnology Laboratory

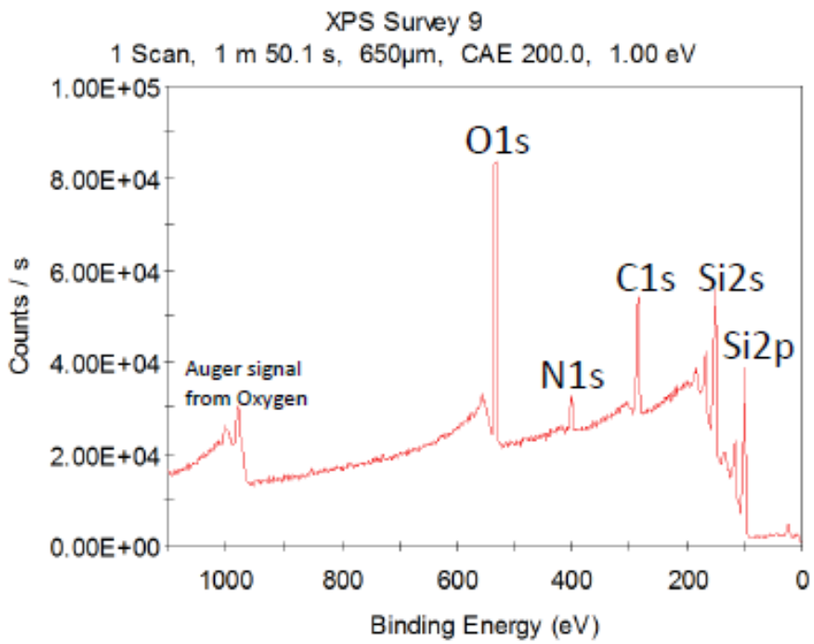
Menu

CHEMICAL COMPOSITION

Polymers

XPS: X-ray Photoelectron Spectroscopy (XPS) is a well-established surface analysis tool. XPS is used to examine the surface elemental and chemical composition, providing atomic composition (excluding H and He) with detection limits in the 0.1 to 1% range.

TGA: Thermogravimetric Analysis (TGA) is a thermal analysis technique involving the determination of the change in weight of a sample as a function of temperature and/or time of heating.



➢ **Composition:**

Name	Peak BE	Atomic %
O1s A	532.88	26.78
C1s A	285.06	6.29
C1s B	285.76	11.32
C1s C	287.01	8.77
Si2p3 A	99.55	28.65
Si2p B	103.21	8.4
C1s D	288.89	3.55
N1s A	399.02	0.36
N1s B	400.88	5.16
N1s C	403.1	0.58
N1s D	407.31	0.14

XPS measurements to follow surface functionalisation

Credits: Alexandra Teixeira, Alex Bondarchuk, International Iberian Nanotechnology Laboratory

Next

CHEMICAL COMPOSITION

Elemental concentration

ICP-OES: inductively coupled plasma optical emission spectrometry (ICP-OES), is an analytical technique used for the detection of chemical elements. It is a type of emission spectroscopy that uses the inductively coupled plasma to produce excited atoms and ions that emit electromagnetic radiation at wavelengths characteristic of a particular element.

EDX: EDX can be used to determine the crystal phase(s) in a layer or in a powder.

XPS: XPS is used to examine the surface elemental and chemical composition, providing atomic composition (excluding H and He) with detection limits in the 0.1 to 1% range.

Impurities (organics)

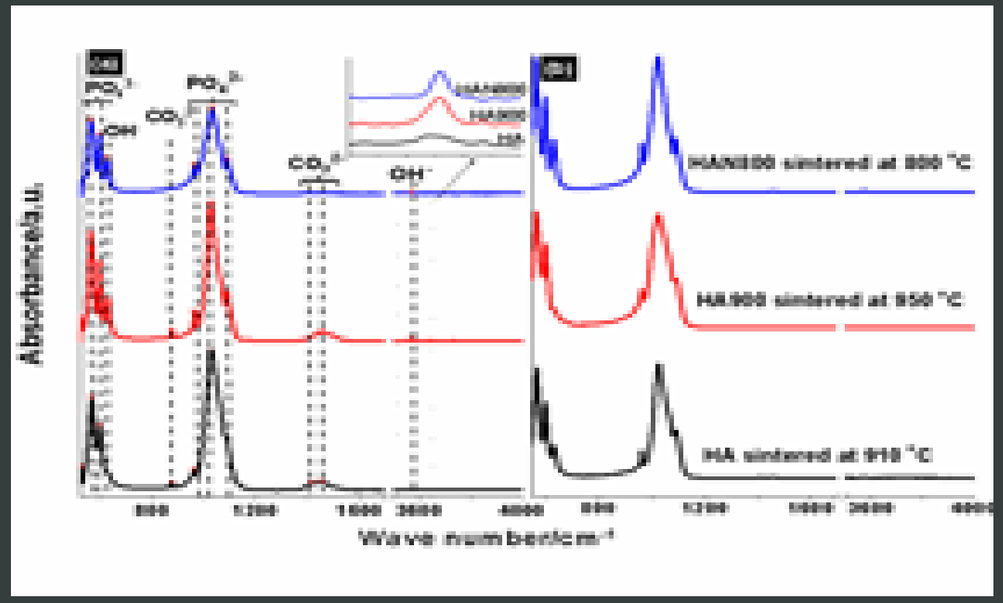
LC-MS/MS: LC-MS/MS is a HPLC unit with two mass spectrometry detectors. The LC is able to separate compounds. The mass spec detector measures the mass-to-charge ratio of ions by exposing the ions to a magnetic or electric field which can alter the movement of the ions allowing the ions to be sorted based on their mass. The mass spectrum of the sample can be used to determine the concentration of compounds, find the mass of impurities and give insight into chemical structures.

Next

CHEMICAL COMPOSITION

Functional Groups

FTIR/ATR-FTIR: Fourier-transform infrared spectroscopy (FTIR) is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high-resolution spectral data over a wide spectral range.



FTIR spectra of hydroxyapatite (a) powders and (b) sintered samples

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

Lipids

HPLC: Due to the structural diversity of the many classes of lipids, HPLC separations can be performed using a variety of chromatographic conditions, with reversed-phase and normal-phase being the most widely used.

Elemental phase composition

ICP-MS: inductively coupled plasma mass spectrometry is a sensitive analytical technique used to identify and quantify the elemental composition of samples, including metals and select nonmetals with atomic masses from 7-250.

Menu

DRUG LOADING / RELEASE

Free vs Encapsulated drug

HPLC-MS: separate each component of a material to determine its concentration.

fluo-NTA: particles loaded with fluorescently labelled drugs and/or fluorescent particles (liposomes, extracellular vesicles) are counted and compared to the total count of particles based on their scattering. NTA records the brownian motion of nanoparticles in solution to determine size and concentration.

small-particle flow cytometry: particles loaded with fluorescently labelled drugs and/or fluorescent particles (liposomes, extracellular vesicles) are counted and compared to the total count of particles based on their scattering. sp-FCM records scatter and fluorescent properties of particles passing a laser one by one in a focused stream.

Evaluation of internal particle structure changes after drug loading

HPLC: HPLC separations can be performed using a variety of chromatographic conditions, with reversed-phase and normal-phase being the most widely used.

SAXS: it can determine nanoparticle size distributions, resolve the size and shape of macromolecules, determine the internal structure of materials, determine pore size and characteristic distances of partially ordered materials.

Drug release in complex media

HPLC-MS - uses a column with different phases and high pressures to separate each component of a material to determine its concentration.

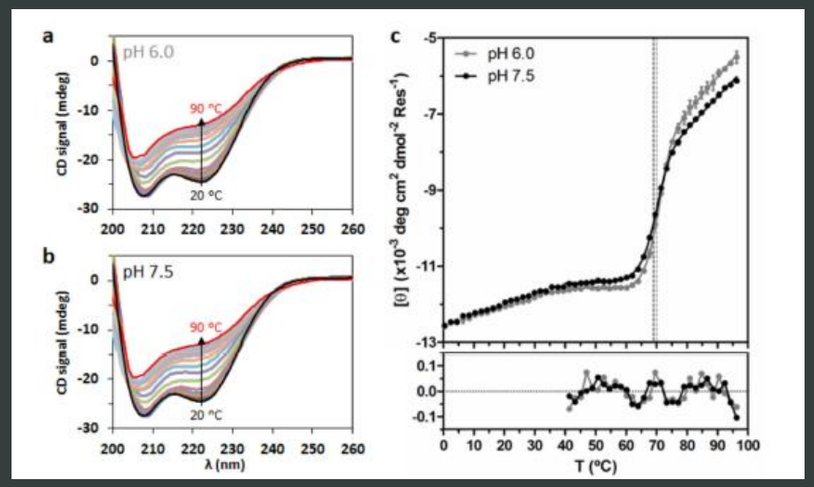
LC-MS/MS: drug release assay utilizing a stable isotope tracer

Menu

OPTICAL CHARACTERISATION

Circular Dichroism

Circular dichroism (CD) spectroscopy is a form of light absorption spectroscopy that measures the difference in absorbance of right- and left-circularly polarized light (rather than the commonly used absorbance of isotropic light) by a substance. CD can be used to estimate the structure of unknown proteins and monitor conformational changes due to temperature, mutations, heat, denaturants or binding interactions.



Protein temperature denaturation followed via circular dichroism

Credits: André Faustino, Instituto de Medicina Molecular

FACS

Fluorescence-activated cell sorting (**FACS**) is a specialized type of flow cytometry. It provides a method for sorting a heterogeneous mixture of biological cells into two or more containers, one cell at a time, based upon the specific light scattering and fluorescent characteristics of each cell. Determines the optical properties of individual events.

High Content Screening

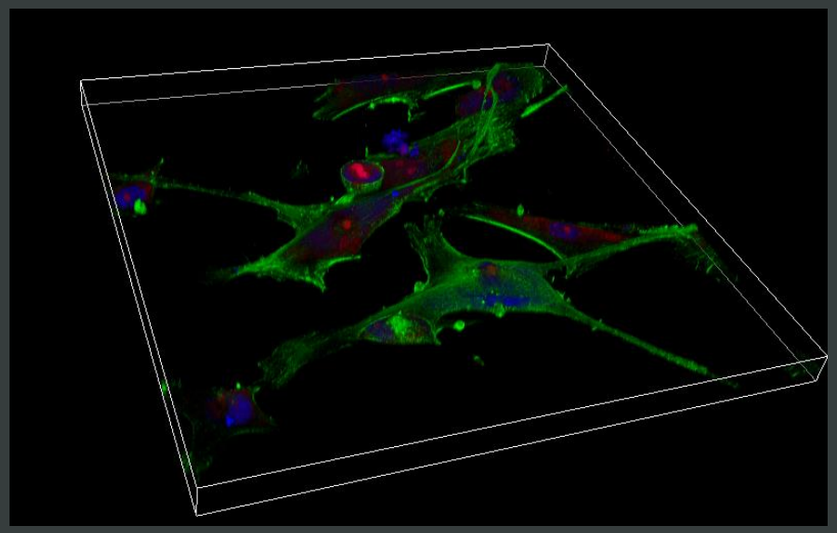
Automated imaging technique for cellular response to materials. Particles / cellular endpoints. Visualizing and quantifying cellular uptake and cytotoxicity

Next

OPTICAL CHARACTERISATION

Confocal Microscopy

Confocal microscopy increases effective spatial resolution by eliminating out-of-focus light, using a point illumination source paired with a pinhole detector aperture. It allows the visualization of cellular interactions and response to materials, the quantification of cellular uptake and cytotoxicity.



3D confocal reconstruction of normal human dermal fibroblasts (nuclei red and cytoskeleton green).

Credits: BforDev Lab and microscopy CGS, UNIPV

Epifluorescence Microscopy

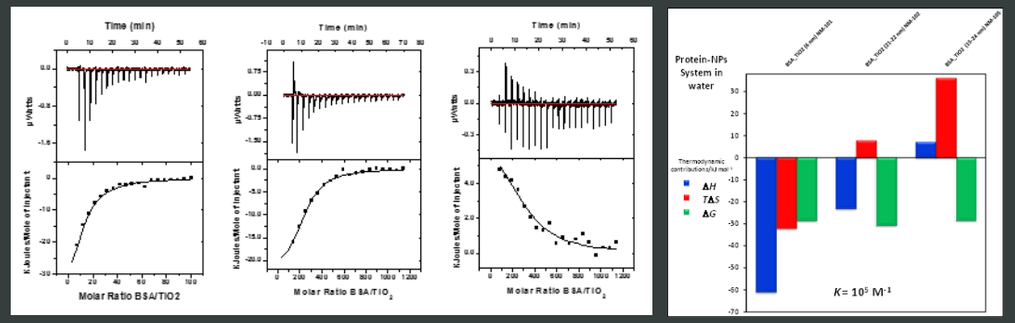
In epifluorescence microscopy, a parallel beam of light is passed directly upwards through the sample, maximizing the amount of illumination.

Menu

BIO-NANOINTERACTION STUDIES

Biomolecule-NP interaction

Isothermal Titration Calorimetry (ITC): ITC can provide useful thermodynamic parameters (Kb, binding constant;- n, stoichiometry, binding enthalpy, entropy; and Gibbs energy of binding) of biomolecules-ligand interaction under native conditions, without the use of tags or labels that may otherwise interfere with binding

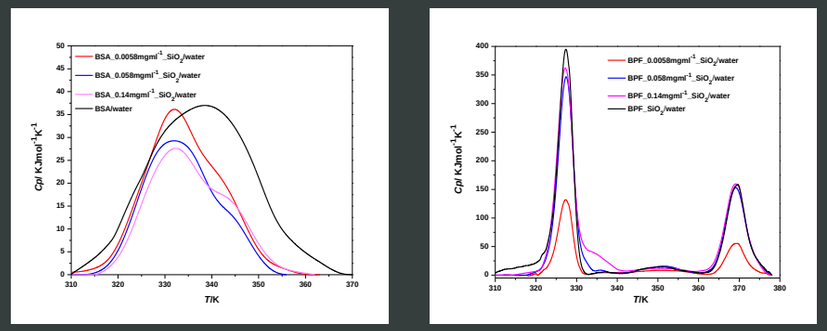


The Binding isotherms for the interaction of Bovine serum albumin (BSA) with three JRC TiO_2 nanoforms having different particle size and crystalline structure: (A) TiO_2 anatase 5-6 nm; (B) TiO_2 anatase 35 nm; (C) TiO_2 rutile - anatase 24 nm.

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

Surface plasmon resonance (SPR) spectroscopy: From the SPR data, the association / dissociation constants (Ka, Kd) at equilibrium as well as the association and dissociation rate constants (ka, kd) of the reaction are determined.

NanoDSC: Thermodynamic investigations of biomolecules (proteins) stability during the Bio-NP interaction.



The heat capacity versus temperature profiles for the thermal denaturation of Bovine serum albumin (BSA) and Bovine plasma fibrinogen (BPF type I-S) in the absence and presence of SiO_2 NPs at different concentrations.

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

Next

BIO-NANOINTERACTION STUDIES

Biomolecule adsorption, biocorona size

Centrifugal particle sedimentation (CPS): sizing based on size and density of the material: thickness of the biocorona can be calculated from a change in the apparent NP size.

NPs' biocorona composition

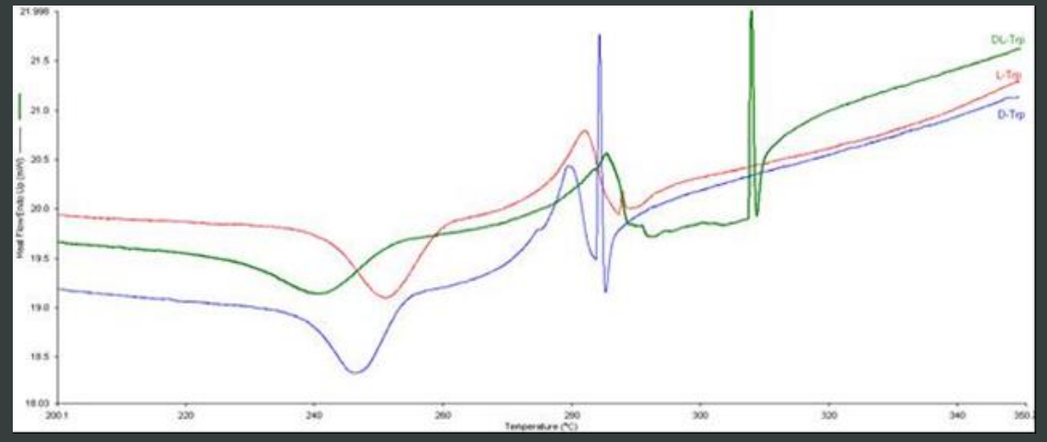
LC-MS-based proteomics with dedicated data analysis workflows

Menu

FORMULATION DEVELOPMENT AND MANUFACTURING

Stability Studies

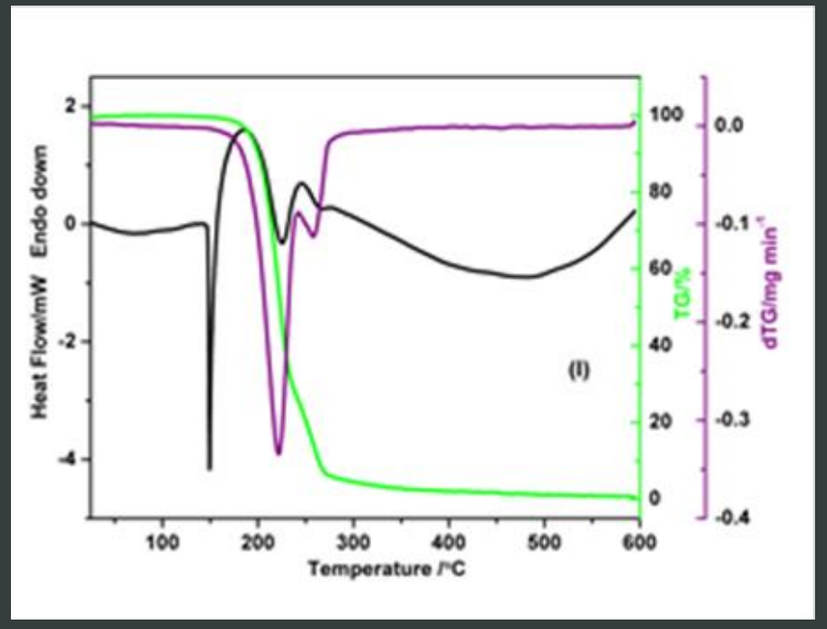
Stability of the active or the final pharmaceutical form based on thermochemical properties of pharmaceutical forms: Differential Scanning Calorimetry (DSC)



DSC curves of L-, D- and DL-Tryptophan

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

Thermogravimetric study of pharmaceutical forms (the mass variation of a sample over time with the temperature changes): Thermogravimetry-Thermal analysis (TG-DSC) .



DSC-TG-dTG curves of N-(p-chlorophenyl)-N'-(2-thenoyl)-thiourea

Credits: Institute of Physical Chemistry "Ilie Murgulescu" (IPCIM)

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FORMULATION DEVELOPMENT AND MANUFACTURING

Solubility

Design & development of pharmaceutical forms

Pulmonary formulations

Size and number concentration of particles in formulations for pulmonary delivery (aerosols and nebulized)

Microparticle and nanoparticles production and chimerical agglomerate of nanosystems

Nanofiber production and nanoparticles in nanofibers

Production of sponge-like systems loaded with nano

Evaluation of surface tension

Identification of chemical modification by FTIR

Menu

COMPUTING

High computing remote access to HPC

Software installation on demand

Massive parallel processing

Mass storage

Onsite & Remote

MODELLING

Physiologically Based Pharmacokinetic (PBPK) modelling

Computational representation of coating nanoparticle release from the implant and prediction of distribution locally and systemically

3-Dimension representation of coating nanoparticle diffusion and implant interaction in tissue

Biomedical signals processing and modelling especially in cardiology

Modelling of the functional behaviour of tissues and organs

Mechanical modelling of tissues and devices in soft tissue

Menu

CYTOTOXICITY

Cytotoxicity (necrosis) by MTT, alamar blue and LDH assay

LLC-PK1 Kidney cells (porcine)

Hep G2 hepatocarcinoma (human)

Normal and Saos-2 human osteoblast

CaCo-2: MTT and permeability (TEER)

Tenocytes primary (tendon cells)-MTT

GL261 cells from mouse glioblastoma (mouse)

Normal lung fibroblast-CCL171

Osteosarcoma MG-63 (human)

Phagocytic cell line (THP-1 or RAW 264,7)

Cell lines selected depending on the exposure route

MTT assay, CCK-8

Cytotoxicity (apoptosis) - Caspase 3 (3/7) Activation assay

LLC-PK1 Kidney cells

Hep G2 hepatocarcinoma

A549 alveolar epithelial cell line cytotoxicity assays

Cytotoxicity of nano-aerosols: MTS and LDH assay

Cytotoxicity assay on lung models exposed at air-liquid interface (A549, BEAS-2B, 3D MucilAir)

A549 alveolar epithelial cell line cytotoxicity assay

Annexin V/PI

LLC-PK1 Kidney cells and Hep G2 hepatocarcinoma

Menu

GENOTOXICITY

Mutagenicity/Genotoxicity

Comet Assay LLC-PK1 Kidney cells and Hep G2 hepatocarcinoma

Mouse lymphoma test

Bacterial Reverse Mutation Test

In vitro Micronucleus Test (OECD 487)

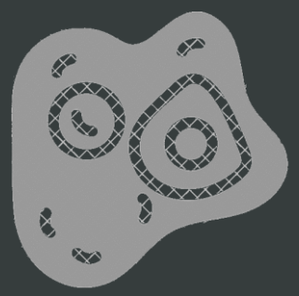
In vitro Tests Using the Thymidine Kinase Gene (OECD 490)

In vitro Mammalian Alkaline Comet Assay (OECD 489**)**

Reproductive toxicity assay

Carcinogenicity assays

Menu



CELLULAR UPTAKE

Internalization studies with confocal microscopy

GL261 cells (Mouse glioblastoma and other cell types)

A549 lung cells, THP-1 monocytes, primary hematopoietic progenitor cells, primary derived dendritic cells

Optical analysis HR dark field optical microscope with spectral analysis (nanoscale optical microscope)

Cytotoxicity and cell uptake by High content screening for multiparametric analysis

Digital imaging by Cells stained for multiple viability markers

Optical measurement of inorganic elements

By ICP-OES- TCD

In vitro cell exposure, cell counting and ICP-MS on cell pellets

Of metallic NPs/Fe-staining

Cell uptake by flow cytometry

A549 lung cells, THP-1 monocytes, primary hematopoietic progenitor cells, primary derived dendritic cells

Menu

IMMUNOLOGY

Complement activation by EIA (ELISA of complement activation markers: C5b-9, iC3b, Bb, C4d)

Plasma coagulation times:

Analysis of nanoparticle Interaction with plasma proteins: NP interaction with plasma proteins by 2D PAGE

Analysis of Hematologic properties of NP

Platelet aggregation analysis

by cell counting

By Light Transmission Aggregometry

Detection of Antibodies (anti-PEG and others)

Immunotoxicity assay *ex vivo*

Proinflammatory macrophages (M1), anti-inflammatory macrophages (M2), dendritic cells, NK cell, lymphocyte.

Detection of nitric oxide production by RAW 264. 7 macrophage cell line

Chemotaxis assay

Phagocytosis Assay

Measurement of nanoparticle effects on cytotoxic activity of NK cells

Lymphocyte proliferation

Menu

HEMATOLOGY

Hematologic properties

- Hemolysis
- Coagulation time
- Platelet adhesion

Leukocyte proliferation assay

Induced inflammatory cytokines

- Analysis of Cytokines, chemokines and Interferons, IL8, IL-1b, TNF-α, IFN ϒ by ELISA of multiplex
- Analysis of Cytokines, Chemokines and Interferons by Multiplex electrochemical protein assay

***In vitro* induction of Leukocyte procoagulant activity**

Determination of cytokine concentrations

- By ELISA kits: detection of different cytokine in culture supernatants
- By Flow cytometry

Inflammasome activation

- Measurement of Il-1b, IL8 secretion, assessment of caspase 1 activity and ASC speck formation by flow cytometry and Luminex

Menu

OXIDATIVE STRESS

Gluthatione Assay with HEP2 Hepatocyte

Lipid Peroxidation Assay with HEP2 Hepatocyte

Reactive Oxygen Species (ROS) Assay Assay with HEP2 Hepatocyte

Intracellular ROS production by nano-aerosols

DCF assay on lung models exposed at air-liquid interface (A549, BEAS-2B, 3D MucilAir)

AUTOPHAGY

Autophagic Dysfunction Assay

Qualitative Analysis of MAP LC31 to LC3-II Conversion by Western Blot

Autophagic Dysfunction in LLC-PK1 cells

Pyroptosis

Cell health

ROSS

Mitochondrial membrane polarization

Gluthatione in primary human immune cells and cell lines

Menu

ORGANS TOXICITY

Human monoculture cell lines:

Gut

Cell health and viability assays- Caco-2

Lung

Cell health and viability assays - Human Bronchial Epithelial Cells (HBEC)

Human lung cell transformation assay

Toxicity testing on lung models exposed at air-liquid interface (A549, BEAS-2B, 3D MucilAir)

Cytotoxicity (MTS and LDH assay)

Oxidative stress (DCF assay)

Inflammatory cytokine production

Gene expression

Eye

Serious eye irritation

Reconstructed human tissue (RhT)-based test. EpiOcular™ EIT 1

Skin:

Skin corrosion and irritation by Reconstructed Human Epidermis (RhE) Test Method

EpiSkin™, skin sensitization by human cell line activation test (KE3) and U937 Skin Sensitisation Test (U-SENS™ assay) (KE3)

Assessment of permeability through cell monolayers by LC-MS/MS or other quantitative approaches:

Intestinal absorption-Caco-2 cells

Capillary penetration-EaHy.926

Cell uptake to represent RES system

Non-mammalian toxicological models:

Acute toxicity in *C. elegans* (LD50)

Chronic toxicity in *C. elegans*

Oxidative Stress in *C. elegans*

Menu

STERILITY

Microbial contamination

- Microbial colonies counted
- Bioburder: quantify the microbial contamination in medical devices
- Detection of bacterial contamination
- Detection of mycoplasma contamination
- Sterility evaluation in medical devices

Endotoxin contamination

- Gel clot, chromogenic or turbidimetric
- LAL assay and HEC293 method
- Validation by LCMS
- NP dispersions for in vitro application: LAL assay (Absorbance), EndoLISA (fluorescent), or Western blot

Pyrogenicity caused by non endotoxin contaminants

OTHERS

PCR on multiple gene expression

- Bcl2
- BAX
- Interleukines
- Chemokines
- Extracellular matrix proteins

Cell Proliferation ELISA

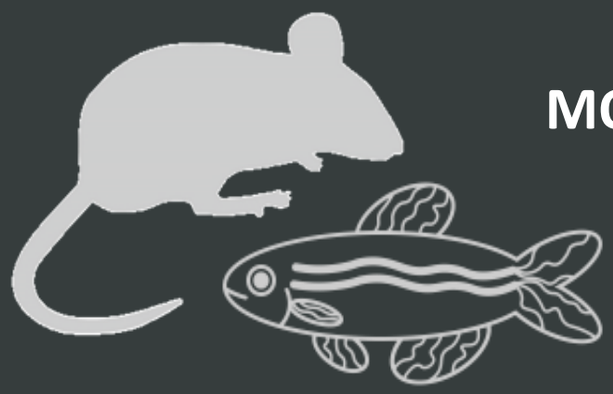
Migration Assay

Adhesion and spreading

Invasion Assay

Wound healing assay

Menu



MODELS OF DISEASE

Click for more details

Next

- Alzheimer disease
- Parkinson disease
- Depression induction
- Schizophrenia
- Rett syndrome disease
- Multiple sclerosis disease
- Experimental autoimmune
- Encephalomyelitis induction
- Spinal cord injury
- Epilepsy of absence
- Cerebral Ischemia

NEUROLOGY

- Crohn's disease
- Psoriasis induction
- Chronic wound
- Colitis induction
- Diabetes
- Obesity
- Niemann-Pick type C disease
- Arthritic disease
- Collagen-induced arthritis
- Adjuvant induced Arthritis

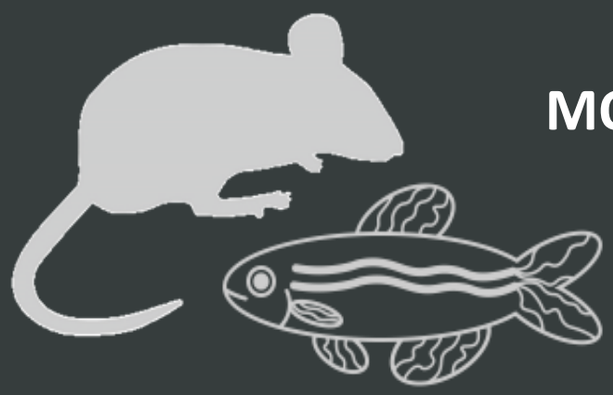
IMMUNOLOGY
INFLAMMATION

- Plasmodium berghei
- Trypanosoma spp.
- Herpes virus
- Pseudomonas aeruginosa
- Klebsiella pneumoniae
- Nippostrongylus brasiliensis
- Listeria monocytogenes
- E. coli infection
- Eimeria vermiformis
- Candida albicans
- Urinary tract infection

INFECTION

Click for more details

Menu



MODELS OF DISEASE

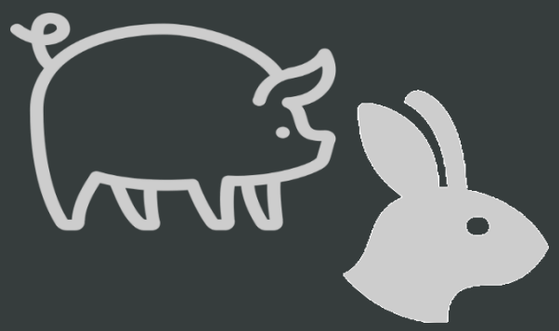
- Colorectal - orthotopic, subcucaneous, intrasplenic
- Orthotopic colon cancer induction
- Pancreas - subcutaneous
- Endometrium
- Glioblastoma
- Orthotopic (steroatactic) - subcucaneous
- Lymphoma
- Leukemia
- Acute myeloid leukemia induction
- Prostate - orthotopic, subcucaneous
- Cervix - subcutaneous
- Lung - subcutaneous
- Ewing sarcoma - subcutaneous
- Melanoma - subcutaneous and intravenous.
- Glioblastoma
- Mamary fat pad tumor induction
- Cerebral metastases
- Breast - breast, breast ductal carcinoma, adenocarcinoma and ductal adenocarcinoma
- Patient-derived tumor graft (PDX) models

ONCOLOGY

ASSAYS

- Validation of contrast agents for MRI, ex vivo, luminescence, CT or echography
- Therapeutic index of drug-loaded nanoparticle and effect
- Occupational Safety testing
- *In vivo* inflammation test
- *In vivo* toxicity
- Acute systemic toxicity test (nanoparticles, medical devices, evaluation of implantation effects)
- Immunotoxicity studies
- Toxicity Studies of Anticancer nanomedicines
- Detection of immune response: detection of antibodies (anti-PEG and others)
- PK of therapeutic antibodies
- Efficacy studies

Menu



MODELS OF DISEASE

Click for more details

Menu

- Diabetic ulcers in córnea
- Ocular pathologies
- Skin ulcers
- Diabetic ulcers in cornea

RABBIT

- Unilateral and bilateral cryptorchidism
- Benign prostatic hiperplasia

DOG

Endometriosis

SHEEP

- Hernias
- Colecystitis
- Urethral obstruction and stenosis
- Endothelium inflammation
- Myocardial infection
- Vascular stenosis
- Arterial embolization
- Aneurysms
- Skin ulcers (diabetic)
- Ulcer
- Diabetes (type II)
- Pseudotumors

PIG

ASSAYS

- Biodistribution studies of pharmacological release in nanotechnological systems
- Pharmacokinetic studies
- Toxicity and immunotoxicity studies
- Histopathology - local tissue and systemic effects
- Surgical procedures
- Biomechanical test (torque, compression)
- Cutaneous irritation and intracutaneous reactivity, pyrogenictiy and implantation effects
- Biocompatibility
- Primary stability
- Performance Study – implants
- Surgical procedure
- Anatomical procedure
- Characterisation with micro CT and densitometric analysis
- Osstell monitoring
- Biomechanical characterisation – compression test and biomechanical tests
- *In vivo* monitoring - Fluorescent or bioluminiscence Xtreme: MRI and CT
- Morphological studies of different materials by light microscopy - SEM and TEM
- Gene expression, protein expression, cell damage of the area, foreign body reaction - qRT-PCR, western, immunohistochemistry, immunofluorescence
- Hemocompatibility: hemolysis, coagulation time, platelet adhesion.
- Monitoring blood pressure, acute markers, inflammatory markers, NP biodistribution, acute systemic toxicities – Iron oxide NPs.
- Evaluation of sensitization with medical devices

Menu

AFFINITY MOLECULES DEVELOPMENT

Production and Validation

Oligonucleotides synthesis service (Custom oligonucleotides and chemical modifications)

Antibodies synthesis service (Pab, Mab production, conjugates)

Peptides synthesis service (Custom peptide synthesis and chemical modifications)

Recombinant proteins Production platform and upscale

Antipeptide-antibodies synthesis service

Quantification/Qualification/Analyses

Oligonucleotides

Depolymerisation and LC-MS/MS for quantitation of oligonucleotides

HPLC-UV

Intact oligo analysis by ESI-FTICR-MS / MALDI-TOF-MS

Antibodies/ Nanobodies

After enzymatic digestion: LC-MS/MS triple quadrupole

Glycosylation: LC-MS/MS triple quadrupole

Menu

CONJUGATION CHEMISTRIES

Surface conjugation chemistries

with antibodies or peptides

NP conjugation chemistries

with proteins or drugs

Protein conjugation

Chemoselective methods compatible with biological systems

BIOFUNCTIONAL CONSUMABLES FOR IVD AND EFFICACY

Device development

Selection of substrate

Biofunctionalisation of surfaces

Design and printing biomedical electrodes

Development of bioanalytical assays for biosensing

Customized 3D scaffolds for cell culture

Menu

IVD DEVELOPMENT

Calibration and quantitative data

Fluidic system of the sensor

Calibration of the sensor

Gene expression/ genotyping: quantitative or qualitative measurements of DNA/RNA biomarkers – dPCR and ddPCR

Quantitative or qualitative measurements of protein biomarkers:

LC-MS and MALDI imaging-based proteomics

Multiplex electrochemical protein assay and ELISA

Real sample analysis and validation

In vitro model sample preparation

Clinical sample preparation

Benchmarking measurements

Quantitative or qualitative measurements of DNA/RNA biomarkers- dPCR and ddPCR

Quantitative or qualitative measurements of protein biomarkers - multiplex electrochemical protein assay and ELISA

Menu

BIOMARKERS DISCOVERY & MONITORING

Continuous monitoring

Co-culture *in vitro* models (GIT models, IPScells, organoids, CRISPR-Cas9)

High-content cell/tissue imaging

Multiplexed immunoassays and immunostaining of cells, tissues and TMAs

Assays on blood, body fluids and isolated DNA, RNA and proteins (PCR, ELISA)

Molecular pathology with qualified pathologists

Organ-on-chip models

Continuous bioreactor

Static discovery

RMN based biomarkers discovery: LC-MS and MALDI imaging-based proteomics

MS (FT-ICT / QTOF) non-targeted detection of metabolites and peptides

Digital biomarkers identification

MRI and other radiology instrumentation

Menu

BIOFILM ANTIMICROBIAL PROPERTIES AND EFFICACY

Bacterial adhesion/Biofilm growth

Microbial growth on surface (Biofilms), cell metabolism on surface, molecule-molecule interaction on surfaces

Bacterial adhesion to materials and formation of biofilms - biomass biofilm, viability bacteria in biofilm in time

Antibacterial activity of materials and coatings

Observation by SEM

Fluorescence live/dead test

Antimicrobial activity under dynamic contact conditions

Antibacterial activity assessment of textile materials

Antimicrobial activity on plastics and other non porous

Antimicrobial activity on polymeric or hydrophobic materials

Efficacy studies

Monoculture cell models (disc, scaffolds)

Bone cell lines

Osteoblast Saos-2: cell adhesion and proliferation onto the coated surface in comparison to uncoated one - SEM/CLSM (staining for cell nuclei/cytoskeleton/extracellular matrix)

Tenocytes, fibroblasts, Saos-2, mesenchymal stem cells: cell adhesion and proliferation onto the coated surface in comparison to uncoated one - SEM/CLSM (staining for cell nuclei/cytoskeleton/extracellular matrix)

Menu