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PROGRAMA IBEROAMERICANO
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CIENCIA Y TECNOLOGÍA PARA EL DESARROLLO

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Nanomedicina: Desenvolvimento de Ferramentas Analíticas Inovadoras

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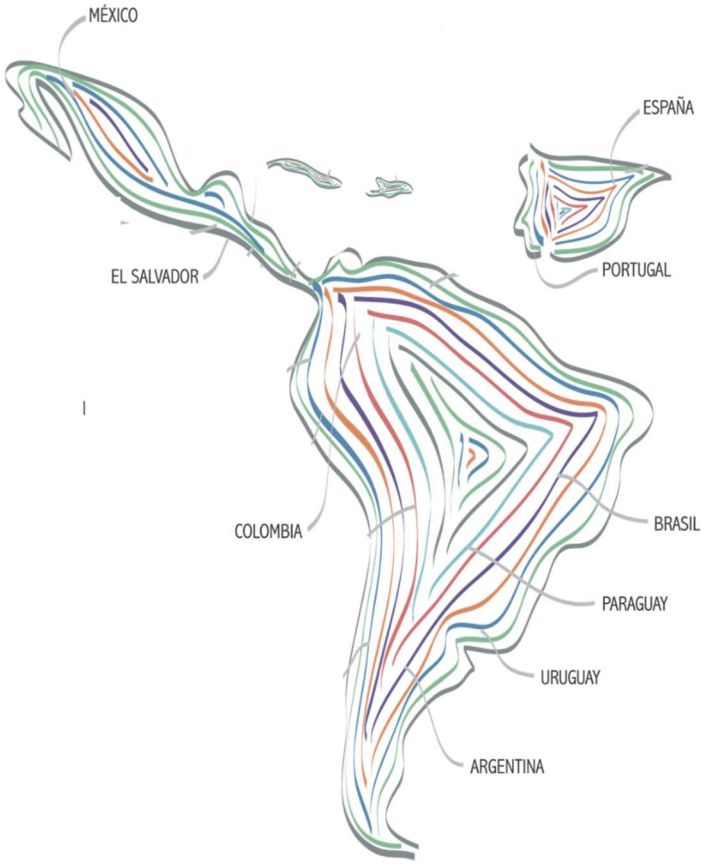
APRESENTAÇÃO DA REDE GENOPSYSENS

DESENVOLVIMENTO DE GENOSSENSORES PARA ALVOS FARMACOGENÓMICOS NO SISTEMA NERVOSO CENTRAL

A rede GEnoPsySEn pretende criar uma equipa de trabalho cooperativo entre países Ibero-Americanos, com o objetivo de definir estratégias para desenvolver dispositivos descartáveis, baratos e de fácil utilização, baseados em genossensores eletroquímicos para detetar polimorfismos genéticos que influenciam a resposta a fármacos associados a doenças do sistema nervoso central (depressão, esquizofrenia, epilepsia e delírios não metabólicos).



A nível mundial existe uma necessidade premente dos clínicos em praticar uma medicina personalizada através da aplicação de terapêuticas individualizadas a cada paciente. Assim, a rede GEnoPsySEn pretende colmatar a lacuna existente nos meios de diagnóstico e criar genossensores precisos que, de uma forma rápida e no local da consulta, possam ser utilizados pelos médicos na prescrição de tratamentos adequados.

Por isso, a GEnoPsySEn pretende contribuir para a transferência de conhecimento entre a academia e o tecido empresarial, assim como para a melhoria dos cuidados de saúde dos países, envolvidos através de uma estreita articulação com serviços nacionais de saúde da rede GEnoPsySEn.

Programa

Todas as sessões se realizarão na Universidade de Quíndio
Sala de Reuniões

20 de agosto de 2025

9:00	**Sessão de abertura**		
9:15	**Estratégias para o desenvolvimento de eletrodos de baixo custo para aplicações em sensoriamento eletroquímico**	**Carla Eiras**	Universidade Federal do Piauí Brasil
9:45	**Sistemas nanoestruturados a base de polissacarídeos modificados: valorização de produtos naturais**	**Durcilene Alves da Silva**	Universidade Federal do Delta do Parnaíba, Brasil
10:15	**Valorización de matrices naturales a través de tecnologías verdes y nanotecnología: compuestos bioactivos, salud cognitiva y aplicaciones en alimentación funcional**	**Miguel Prieto & Maria Carpena**	Universidade de Vigo, España
10:45	*Pausa para café*		
11:15	**Vesículas Extracelulares: Estratégia Inovadora em Nanomedicina**	**Ana Teixeira**	Centro de investigação do Instituto Português de Oncologia do Porto - Portugal
11:45	**Genossensor eletroquímico para detetar SNP no CYP2D6**	**Fátima Barroso**	REQUIMTE/LAQV-ISEP Portugal
12:15	***Almoço***		
14:00	**Mesas redondas e discussão dos temas**		
17:45	***Fim***		

22 de agosto de 2024

9:30 - 16:00	Reuniões da REDE CYTED – GENOPSYSENS Discussão aberta sobre os planos de trabalho para o 4º ano de projeto.

RESUMOS

EVALUATION OF THE INFLUENCE OF *CYP2C19* AND *CYP2D6* GENE POLYMORPHISMS ON ESCITALOPRAM AND PAROXETINE THERAPY IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN THE STATE OF PIAUÍ, BRAZIL

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Major depressive disorder (MDD) is a serious public health issue affecting millions of individuals worldwide, with high rates of morbidity and mortality. It is the leading cause of disability globally, with Brazil being the second country with the greatest economic losses due to reduced productivity. Despite advances in treatment, the effectiveness of antidepressants – particularly selective serotonin reuptake inhibitors (SSRIs) – varies significantly among patients, partly due to genetic differences in drug metabolism. Escitalopram and paroxetine are among the most widely prescribed SSRIs and are primarily metabolized by the cytochrome P450 enzymes CYP2C19 and CYP2D6, whose activity is modulated by common genetic polymorphisms such as *CYP2C19* *2, *3, *17 and *CYP2D6* *4, *10, *41, *17. This project aims to investigate the influence of these polymorphisms on the metabolism of escitalopram and paroxetine, and their relationship with therapeutic response in patients with MDD from the state of Piauí, Brazil. The study objectives include: (1) determining allele and genotype frequencies of the polymorphisms in a representative sample of the Piauí population; (2) assessing the bioavailability, efficacy, and safety of escitalopram and paroxetine in MDD patients; and (3) correlating genotypic profiles with pharmacokinetic and clinical data collected over an eight-week period. The methodology comprises two complementary studies: a molecular-epidemiological investigation and a pharmacogenetic association study. For the epidemiological component, healthy individuals born in Piauí will be recruited, with proportional representation from the state's four mesoregions. The pharmacogenetic study will include patients diagnosed with MDD undergoing treatment with SSRIs for at least eight weeks. Peripheral blood samples will be collected for DNA extraction and genotyping of polymorphisms using quantitative polymerase chain reaction (qPCR). Plasma concentrations of SSRIs will be quantified via HPLC-MS/MS, while treatment efficacy and safety will be evaluated using standardized psychological assessment tools (Hamilton Depression Rating Scale, Beck Depression Inventory, and UKU Side Effect Rating Scale). Expected outcomes include the determination of allele and genotype frequencies of *CYP2C19* and *CYP2D6* polymorphisms in the Piauí population, as well as the identification of metabolic profiles associated with therapeutic response to SSRIs. The findings are expected to enable correlations between metabolizer phenotypes (e.g., poor, intermediate, or ultra-rapid metabolizers) and treatment efficacy or adverse effects. These insights may contribute to cost-effective personalized antidepressant therapy through dose optimization and risk reduction. Furthermore, this study represents a significant step toward implementing precision medicine strategies in the psychiatric treatment of patients in the region, enhancing the understanding of pharmacogenetic determinants of interindividual variability in SSRI response, and improving the quality of life of patients with MDD, ultimately generating a positive impact on public health.

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Acknowledgments

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APLICACIÓN DE LAS VESICULAS EXTRACELULARES EN EL DIAGNÓSTICO Y TRATAMIENTO DE ENFERMEDADES NEUROLÓGICAS

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Las vesículas extracelulares (VE) han provocado un gran interés en dilucidar los paradigmas relacionados con la activación y silenciamiento de vías de señalización. Las vesículas extracelulares se dividen principalmente en exosomas y microvesículas dependiendo de su biogénesis, tamaño y composición; su principal función es transportar proteínas de señalización, diferentes tipos de RNA, DNA y lípidos. Una vez liberadas, su contenido es absorbido selectivamente por células cercanas o distantes, para influir en su comportamiento. Los exosomas participan en la comunicación intercelular en una amplia gama de procesos del desarrollo embrionario y en la comunicación materno-fetal, también tienen una participación importante en el desarrollo neuronal, la regeneración y enfermedades. Las VE en células sanas actúan como reguladoras de la homeostasis normal, pero en condiciones patológicas pueden promover la neuroinflamación, degeneración o la reparación tisular, dependiendo de las moléculas presentes en su contenido. Por este motivo, las vesículas extracelulares se han propuesto como una herramienta para el diagnóstico de diversas enfermedades tanto sistémicas como del sistema nervioso central (SNC) por su capacidad para atravesar la barrera hematoencefálica (BHE). Además del diagnóstico de enfermedades, estas vesículas también se han utilizado en la administración dirigida de fármacos capaces de atravesar la BHE para el tratamiento de enfermedades que afectan al SNC.

De acuerdo con la clasificación 2021 de la Organización Mundial de la Salud, los gliomas difusos del tipo adulto incluyen astrocitomas grado 2 al 4 que se caracterizan por presentar mutaciones específicas en variantes de la enzima isocitrato deshidrogenasa para la producción del oncometabolito alfa-cetoglutarato y la ausencia de la proteína nuclear ATRX. A pesar de los avances tecnológicos en la cirugía de los gliomas y el uso de tratamientos complementarios de quimioterapia y radioterapia, hasta el momento no existe cura para este tipo de tumores. Por ello, se siguen buscando alternativas de tratamiento y una de las opciones preclínicas más utilizadas es el modelo murino de glioma por xenotrasplante. Para el desarrollo de este modelo se realiza un transplante intracrateal de 50,000 a 200,000 células de la línea celular de glioma de rata C6 en la corteza cerebral, para desarrollar un tumor grado 4 de estirpe astrocítica después de 3 semanas de evolución. En un trabajo publicado por nuestro grupo se observó que la administración de vesículas extracelulares artificiales conocidas como liposomas a los que se les cargaron compuestos antineoplásicos, pueden ser una alternativa de tratamiento para los gliomas. La quercetina o Quer es un flavonoide con propiedades antiinflamatorias, antioxidantes y antineoplásicas. El 3-Bromopiruvato o 3BP es un compuesto alquilante similar al piruvato que inhibe la hexoquinasa II y al gliceraldehído-3-fosfato deshidrogenasa, su acción citotóxica en células tumorales está asociada a la autofagia. Los resultados mostraron que la administración intraperitorial de liposomas cargados con 1 mg/kg de Quer + 1.5 mg/kg de 3BP, inhibió el crecimiento tumoral y aumentó la sobrevida de los animales. Como conclusión, esta formulación podría ser una opción de tratamiento para pacientes con glioma a los que se les realizó una resección tumoral amplia (>90%) por su capacidad de inhibir el crecimiento tumoral.

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Acknowledgments

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IMPACTO DE LA NANOMEDICINA EN EL ABORDAJE TERAPÉUTICO DE LAS ENFERMEDADES NEURODEGENERATIVAS

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La nanomedicina utiliza materiales y dispositivos a escala nanométrica desarrollados para interactuar a nivel molecular con el cuerpo humano, lo que ha permitido su aplicación en cuatro grandes áreas: el nanodiagnóstico, la nanoterapia, la prevención y la nanomedicina regenerativa. En las últimas décadas, la nanomedicina ha permitido generar alternativas terapeúticas para las enfermedades neurodegenerativas (END), incluyendo las enfermedades de Alzheimer y Parkinson, la epilepsia, la esclerosis múltiple, la enfermedad de Huntington, la lesión traumática de médula espinal (LTME), el cáncer cerebral y la enfermedad cerebro vascular, al hacer más eficiente la administración de medicamentos en el sistema nervioso central [1]. Lo anterior se debe a que las nanopartículas de diferentes biomateriales pueden actuar como transportadores de fármacos que pueden dirigirse con precisión a las subregiones cerebrales o medulares afectadas, lo que potencia el éxito de la terapia. Algunos biomateriales nanopartículados incluso pueden atravesar la barrera hematoencefálica (BHE) y mejorar la eficacia de los medicamentos. Esto ocurre porque a escala nanométrica los materiales tienen propiedades diferentes desde el punto de vista térmico, eléctrico, magnético y óptico, en comparación con sus características macroscópicas. Aunado a lo anterior y, por lo qeneral, además de su capacidad de cargar fármacos, las nanopartículas tienen alta estabilidad y baja toxicidad.

La nanomedicina aplicada al tratamiento de las END es prometedora, por ejemplo, en la epilepsia, uno de los trastornos neurológicos crónicos más comunes, que pese a la gran cantidad de nuevos fármacos antiepilépticos (FAE) disponibles y en desarrollo que existen, un alto porcentaje de pacientes con epilepsia (35-40%) son resistentes a los fármacos, siendo una posible causa de ello la sobreexpresión de proteínas de resistencia a múltiples fármacos en el endotelio de la BHE, como la glicoproteína P, la que cual evita que los fármacos lleguen a su diana y alcancen concentraciones adecuadas en el cerebro. El uso de nanosistemas y nanotransportadores de FAE puede aplicarse en la epilepsia farmacorresistente, como es el caso de la fenitoína transportada por nanopartículas de óxido de hierro con núcleo de sílice, con lo cual se han reducido las convulsiones en ratas que previamente no responden a este fármaco, pudiendo representar una estrategia prometedora para pacientes con epilepsia farmacorresistente [2,3].

Otro ejemplo es la LTME, donde biomateriales nano y mesoparticulados como el polipirrol dopado con yodo (PPy/I) sintetizado por el método de plasma, han generado resultados positivos sobre la neuroprotección, la neurorregeneración de la médula espinal y la recuperación de las funciones perdidas tanto en ratas como en primates no humanos y sin necesidad de agregar fármacos, moléculas o factores tróficos [4]. La nanomedicina está surgiendo como una herramienta altamente eficaz para superar las barreras que aún desafían a la medicina tradicional, pudiendo ayudar a millones de personas en todo el mundo a superar problemas de salud relacionados con las END.

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ADVANCES IN BIOELECTROCHEMICAL TRANSDUCTION WITH GFETS: TOWARDS THE DESIGN OF GENOSENSORS FOR NEUROPHARMACOGENETIC APPLICATIONS

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Numerous studies have reported the use of graphene-based electrolyte-gated field-effect transistors (GFETs) as transducer elements in electrochemical biosensors. The high sensitivity of graphene to interfacial electric fields and charges enables efficient transduction at low operating voltages, with rapid response times. Essentially, the surface biorecognition event of the target molecule induces a perturbation in the ionic atmosphere over the graphene channel. This physicochemical change in the Debye layer can be detected and, eventually, quantified through the shift of the graphene's Dirac Point. In this work, transfer curve monitoring is employed as the bioelectroanalytical metric, while the analytical parameters evaluated are the variation of the potential and, in some cases, the current at the Dirac Point (ΔE_{DP} and ΔI_{DP}, respectively) for each graphene channel.

Ultrasensitive biodetection using GFETs holds significant potential for clinical diagnostics and monitoring. However, it faces major challenges, including high signal variability and drift in the electroanalytical response. This work contributes new bioanalytical insights by exploring functionalized GFETs, leveraging a robust device architecture and a practical strategy to mitigate signal instability.

In line with previous work by our group [1], we propose the use of miniaturized GFETs (mGFETs) as a multichannel (bio)electrochemical transduction platform, replacing the S-20 design. Both devices are manufactured by Graphenea Semiconductor S.L [2]. The mGFETs contain 14 graphene channels within a 10 mm² area and offer superior analytical reliability due to improved graphene channel quality and better interchannel reproducibility in the electroanalytical signals. For testing, a dedicated interface board developed by Graphenea was used to connect the graphene chip to the measurement equipment (Sourcemeter Keithley 2200). This setup resulted in an improved signal-to-noise ratio and reduced the risk of physical damage or contamination of the graphene channels, thanks to a more stable intermediate electrical connection.

The transduction system also incorporates an external Ag/AgCl mini-reference electrode, providing a more stable reference potential compared to the Gate terminal provided by the manufacturer. Additionally, a stabilization protocol was implemented prior to signal acquisition, consisting of three consecutive transfer curve cycles. As a further enhancement, an automated multiplexer was developed to enable sequential scanning of all channels, along with a custom Python script tailored to the experimental setup to streamline signal acquisition, data processing, and increase overall throughput.

The graphene channels were functionalized using angiotensin-converting enzyme 2 (ACE2) and 1-pyrenebutyric acid N-hydroxy succinimide ester (PBSE) as a linker. Upon evaluating the affinity biosensor through incubation with 300 fg/mL of SARS-CoV-2 Spike protein, a statistically significant response was observed for both analytical parameters (ΔE_{DP} and ΔI_{DP}) compared to the blanks and control samples. A noticeable signal in the presence of BSA was attributed to nonspecific adsorption, likely due to the absence of a blocking step. It is worth noting that ΔI_{DP} exhibited a substantially higher signal-to-noise ratio than ΔE_{DP}. Based on these preliminary results, we propose this mGFET-based transduction platform as a promising alternative for the development of genosensors targeting pharmacogenetic biomarkers of the central nervous system. Within the framework of the GEnoPsySEn-CYTED network, this approach represents a versatile and adaptable strategy to advance the integration of ultrasensitive biosensing technologies into clinical applications for personalized medicine.

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APPROACHES TO THE FABRICATION OF LOW-COST ELECTRODES FOR ELECTROCHEMICAL SENSING

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The development of electrochemical sensors directly depends on the characteristics of the materials employed in their fabrication, as these materials constitute the interface responsible for the transduction of analytical reactions [1]. However, most commercially available electrodes are manufactured with inert and high-cost materials, in addition to involving industrial processes that limit system customization and hinder environmentally appropriate disposal [2]. In this context, the pursuit of sustainable and low-cost sensors constitutes an essential strategy to promote decentralization and expand access to electroanalytical technologies. Accordingly, the use of alternative materials, combined with simplified manufacturing methods, enables cost reduction and the development of sustainable devices adaptable to the specific needs of each application [3]. In our research group, several approaches have been explored with the aim of replacing conventional commercial electrodes with alternatives that are more affordable, sustainable, and compatible with different analytical matrices. Among these strategies, the following stand out: the use of graphite pencil leads as working electrodes; the fabrication of miniaturized electrochemical cells by 3D printing; and the production of stencil-printed electrochemical sensors on alternative substrates, such as paper, acetate sheets, and gelatin-based biodegradable films, combined with conductive inks formulated with carbonaceous materials and eco-friendly solvents. These platforms have proven effective in detecting various analytes in complex matrices. One example is the use of graphite pencil leads for tracking artificial dyes illegally added to fruit pulps such as cajá and passion fruit. Another case involves the quantification of the flavonoids rutin (RU) and quercetin (QCT) in grape samples, using sensors fabricated with gelatin-based biopolymeric films, screen-printed with conductive ink based on carbonaceous materials and gum extracted from *Amburana cearensis*. The analytical curves obtained by differential pulse voltammetry showed excellent linearity in the range of 1 to 100 µM, with detection limits of 0.02558 µM for QCT and 0.009070 µM for RU, demonstrating the high sensitivity of the platform. Recently, we have initiated the development of a sensor using a conductive ink formulation based on graphite and PVC glue, aiming to detect escitalopram, an antidepressant drug belonging to the class of selective serotonin reuptake inhibitors (SSRIs).

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Valorization of Natural Matrices through Green Technologies and Nanotechnology: Bioactive Compounds, Cognitive Health, and Applications in Functional Foods

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Edible plants, agricultural by-products, and macroalgae have gained increasing attention as natural sources due to their richness in bioactive compounds with potential health benefits. These matrices not only serve as abundant and renewable sources of phytochemicals with neuroprotective properties but also align with circular economy strategies aimed at reducing food waste and promoting sustainable valorization. To obtain these target compounds, the application of green extraction techniques, such as pressurized liquid extraction (PLE), supercritical fluid extraction (SFE), microwave-assisted extraction (MAE) or ultrasound-assisted extraction (UAE), has been studied in recent decades. These techniques are characterized by reduced solvent use and shorter processing time, without affecting bioactivity effectiveness, therefore helping to create functional products that are more environmentally friendly (1). Moreover, advanced analytical techniques such as high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS) play a crucial role in the identification and quantification of these bioactive compounds.

Edible macroalgae are characterized by their richness in various bioactive compounds, some of which have attracted growing interest due to their neuroprotective capacity, such as fucoxanthin (2,3). However, these neuroprotective compounds usually show low stability and limited bioavailability, which limits their application in functional food formulation. To overcome this limitation, nanoencapsulation is presented as a feasible strategy to protect, transport, and release these compounds in a controlled manner, enhancing their neuroprotective efficacy. For instance, fucoxanthin has been loaded into PLGA-PEG nanoparticles, showing an increased bioavailability and efficacy against Alzheimer's disease (4), while similar improved bioavailability results were obtained with alginate nanoparticles loading fucoxanthin (5). To date, various functional foods with neuroprotective compounds present in seaweed have been developed, such as "*Ao Nori* Brain Health". This functional product, containing fucoxanthin in its formulation and aimed at improving cognitive health, was the result of the collaboration between academia and industry. Despite its potential, bioavailability, stability and delivery of neuroprotective compounds could be enhanced by incorporating fucoxanthin into nanoencapsulates. These advances demonstrate the promising strategy of combining the valorization of natural matrices, green extraction techniques, and nanoencapsulation to develop functional products within the framework of neuroprotective nutrition strategies.

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Nanomedicine as a potential approach to avoid cancer drug treatment resistance: A. review

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In recent years, cancer has become the first or second leading cause of death in 112 countries, according to data from the World Health Organization (WHO). [1]. This situation has generated growing concern globally and has prompted the development of various strategies to reverse this trend. Among them, addressing drug resistance has become a key priority to improve the efficacy of cancer treatments [1,2]. Acquired drug resistance is defined as the resistance generated after antitumor treatments causing a gradual reduction of the anticancer efficacy of such treatment. To overcome this, nanomedicine has been suggested as a suitable strategy. Concretely, using nanoparticles enables to transport and release the cancer drug treatment in tumor cells more effectively [2]. In this regard, liposomes, polymeric micelles, mesoporous silica, and magnetic nanocarriers, have demonstrated their ability to evade efflux pumps by improving intracellular drug accumulation and enabling endosomal escape [3,4]. Furthermore, studies have shown that surface functionalization of these systems with ligands (*e.g.,* folate, hyaluronic acid, iRGD) enables receptor-mediated uptake in resistant tumor cells, while stimulus-responsive designs (pH, redox, magnetic-, or light-responsive systems) trigger drug release, specifically within the tumor microenvironment [3]. Co-administration of multiple agents, including chemotherapeutics and resistance modulators (e.g., curcumin or ARNi), helps to enhance therapeutic efficacy and prevent adaptive resistance [5]. Therefore, these advances not only improve drug bioavailability and tumor specificity but also enable the resensitization of resistant cancers, offering a more effective and less toxic alternative to conventional therapies [4,5]. Thus, this review discusses the potential application of nanomedicine to reshape cancer treatment paradigms, focusing on the prevention of cancer treatment resistance and evaluating the main limitations of this approach.

Keywords: Nanomedicine; acquired drug resistance; nanoparticles; cancer treatment.

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Antioxidant Activity of *Camellia japonica* Leaf Extracts and Their Potential for Nanomedical Applications

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Camellia japonica, widely recognized for its ornamental value, has recently attracted scientific attention due to its bioactive compounds. While much of the existing research focuses on its flowers, the therapeutic potential of its leaves remains relatively underexplored. These leaves are known to contain various polyphenols and flavonoids, which are linked to antioxidant and anti-inflammatory effects. The aim of this study is to evaluate the antioxidant activity of *C. japonica* leaf extracts and consider their potential for future nanomedical applications. In this study, extracts obtained from the dried leaves were assessed using two common radical scavenging assays: DPPH and ABTS. The calculated IC_{50} values were 33.11 µg/mL (DPPH) and 23.75 µg/mL (ABTS), indicating strong antioxidant capacity. Additionally, the total phenolic content (TPC) of the extract was measured as 36.67 mg GAE/g dry matter, further supporting its bioactivity. Despite these promising results, the therapeutic use of natural antioxidants is often limited by their poor solubility, low stability, and limited bioavailability. In this context, nanotechnology-based approaches such as nanoencapsulation may offer effective strategies to enhance their pharmacological performance by enabling controlled release and targeted delivery. In conclusion, *Camellia japonica* leaf extracts show high antioxidant potential and could serve as promising candidates for future research in nanomedicine, especially in the prevention or management of oxidative stress-related conditions.

Keywords

Camellia japonica, antioxidant activity, phytochemicals, nanoencapsulation, oxidative stress, nanomedicine.

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Exosomes and extracellular vesicles: a new frontier for the targeted delivery of phenolic compounds

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Phenolic compounds, present in fruits, vegetables, legumes, and their industrial by-products (by-products), are the most studied secondary metabolites due to their structural diversity and recognized bioactive properties. Their most significant effects include their antioxidant, anti-inflammatory, and modulatory functions in various cell signaling pathways, which has led to growing interest in their application as preventive and therapeutic agents in chronic non-communicable diseases, especially cancer, neurodegenerative, and cardiovascular diseases [1]. However, their use is limited due to their low bioavailability and poor stability in the body. Various phenolic compounds degrade during digestion, exhibit low solubility, and are unable to cross key biological barriers, making it difficult to achieve effective concentrations in target tissues [2]. Faced with this challenge, research into delivery and controlled-release systems has gained importance. In this context, exosomes and other extracellular vesicles (EVs) are an alternative to overcome these limitations due to their unique characteristics, such as high biocompatibility, low immunogenicity, the ability to cross biological barriers, and the potential for surface modification to target specific tissues or cells [3,4]. In this regard, various experimental studies have demonstrated that it is possible to encapsulate phenolic compounds—such as resveratrol, curcumin, catechins, and quercetin—within exosomes derived from plant or animal cells, increasing their stability against enzymatic degradation and promoting their sustained and localized release [5–7]. Despite their enormous potential, significant challenges remain. Standardizing isolation and loading methods, optimizing yields at pilot scale, and validating safety and efficacy in animal models and clinical trials are aspects that require urgent attention. Furthermore, the lack of clear regulations governing their production and use for therapeutic purposes adds complexity to their technology transfer. This communication discusses the latest advances in this field, present experimental examples, and address the challenges and regulatory prospects for converting exosomes into a viable platform for the targeted delivery of phenolic compounds.

Keywords: Exosomes, extracellular vesicles, phenolic compounds, targeted release, nanomedicine.

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Enhanced nanoparticle-based delivery strategies of resveratrol as anticancer agent

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Resveratrol, a stilbene found in various plants and fruits, has become a phytochemical of great interest for its capacity to enact various significant therapeutic effects such as anti-inflammatory, antiobesity and antitumoral agent. As anticancer agent, it appears to exhibit selective toxicity against tumoral cells both *in vitro* and *in vivo*. Nonetheless, as in the case of many other polyphenols, the potential anticancer effects of resveratrol suffer from low bioavailability and rapid systemic degradation. Thus, to overcome such hurdles, the development of nanoparticle formulations with conjugated resveratrol have shown great promise as not only these tend to exhibit higher bioavailability and prolonged half-life, but also greater antitumoral effects. Various nanoparticle formulation and delivery systems are currently available, either conjugating resveratrol with organic or inorganic molecules, or rather enveloping the molecule with different membranes, which display a differentiated toxicity and effective profile. These include the use of liposomes, micelles, dendrimers, gold or zinc oxide nanoparticles, among other novel nanocarrier systems. Depending on the nanoparticle material and intrinsic properties, and its water solubility, absorption, bioavailability, and sustained release. This communication highlights the latest developments in nanoparticle-based delivery systems for resveratrol, focusing on the potential to overcome limitations associated with the compound's bioavailability and therapeutic effectiveness.

Keywords:
Nanoparticles, cancer, resveratrol, bioavailability, encapsulation, liposomes, nanomedicine.

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ELECTROCHEMICAL MULTITARGET MIRNA BIOSENSORS FOR MONITORING CASTRATION-RESISTANT PROSTATE CANCER

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Prostate cancer is one of the most frequently diagnosed cancers and the fifth leading cause of death among men worldwide [1]. The androgen signaling pathway is crucial in prostate cancer initiation and progression, which makes it a therapeutic target by androgen deprivation therapies (ADT), one of the main treatment strategies for advanced prostate cancer [2].
However, most patients develop resistance, resulting in castration-resistant prostate cancer (CRPC) [3, 4]. Among ADT, enzalutamide contributes to increasing the overall survival of patients with CRPC. However, enzalutamide resistance is currently a major problem, since there are no predictive biomarkers that allow early detection of these forms of resistance and accurate patients' follow-up [5]. Therefore, it is urgent to define new molecular biomarkers that predict the treatment response, as well as biomarkers of treatment resistance to antiandrogen agents.
Recently, microRNAs (miRNAs) have been proposed as promising biomarkers for cancer diagnosis, prognosis, and therapy monitoring due to their stability in circulation and differential expression between normal versus cancer cells [6,7].
Conventional miRNA analysis is labor-intensive and requires expensive instrumentation [8]. The development of highly specific and sensitive electrochemical miRNA-based biosensors can fill the gap in the diagnosis and foster good analytical procedures to help improve CRPC early detection accuracy [9]. Biosensors are used in point-of-care devices since they are portable, simple, easy to use and cost-effective [10]. Despite the advantages, no biosensors have been developed with this aim, which makes this an important field to explore.

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A novel electrochemical nanogenosensor for the detection of *Candida albicans*.

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Considering tremendous progress in the prevention and treatment of fungal illnesses, invasive fungi such *Candida* species continue to be a major cause of morbidity and mortality [1]. Approximately 300 million people get a fungal infection year, and more than 1.5 million of them die, according to the Global Action Fund Infections. *Candida albicans* is the most important fungal 66 opportunistic pathogen, and it can cause superficial or invasive infections [1,2]. *Candida* can enter the bloodstream and propagate to internal organs, but it also frequently leads to surface infections, particularly those in the skin or mucous membranes, which can be readily and effectively treated [3]. It has been reported in high-risk patients, such as those receiving allogeneic stem-cell transplants and those undergoing high-dose chemotherapy for acute leukaemia [4]. These patients are more vulnerable to infections since their immune systems have been compromised during the transplant process. Systemic fungal infections remain challenging to diagnose. Therefore, developing early diagnosis methods that are more precise, sensitive, and effective is required. In order to identify fungal infections in patients following haematopoietic stem cell transplantation (HSCT), this study developed a simple rapid, and accurate method. For the purpose of detecting Candida albicans, an electrochemical nanogenosensor was developed. An innovative inexpensive electrochemical paper-based analytical device (ePAD) was used for manufacturing this nanogenosensor. The electrochemical signal's sensitivity was increased through the application of a sandwich hybridisation procedure. The preliminary results reveal that these nanogenosensors can be used to identify Candida spp. in a synthetic fungus sample. Considering these results, efforts are continuing to optimise the nanogenosensor for the quantification of Candida albicans, a process that will be proven in future studies. Future developments will cover the application in a hospital setting, including sensitivity, accuracy, response time, challenges, and potential.

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Construction of electrochemical genosensors for the identification of the polymorphism (c.100C>T, rs1065852) located in the CYP2D6*10 gene

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Pharmacogenetics enables the personalization of therapy based on genetic variants that modulate drug response [1-3]. The CYP2D6 gene, responsible for the metabolism of various psychotropic drugs, presents the rs1065852 polymorphism, which defines the CYP2D6 10 allele. This allele is associated with an intermediate metabolizer phenotype, resulting in reduced enzymatic activity and an increased risk of suboptimal clinical response.

In this context, a disposable electrochemical genosensor was developed for the rapid and specific detection of the rs1065852 polymorphism. The approach involved immobilizing a 25-base thiolated oligonucleotide sequence on gold screen-printed electrodes (GSPE) via a self-assembled monolayer composed of thiolated DNA (-SH group) and mercaptohexanol (MCH), followed by a sandwich hybridization reaction with a complementary single-stranded DNA sequence labelled with fluorescein and monitored using voltammetric techniques, specifically chronoamperometry.

The developed genosensor demonstrated high sensitivity, selectivity, and reproducibility (RSD of 17.65% and 23.79%). The fully complementary DNA target sequence (Target T) produced an electrochemical signal 56.81% higher than that of the DNA target sequence containing the polymorphism (Target C). These results indicate that the genosensor represents a rapid, precise, and robust analytical tool with potential for clinical pharmacogenetics, enabling individualized optimization of epilepsy therapy.

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Molecularly imprinted Paper-Based Electrochemical Sensor For Hydrochlorothiazide analysis

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The presence of active pharmaceutical ingredients in freshwater environments has become an increasing environmental and public health concern [1]. These compounds enter aquatic systems through various pathways, with Wastewater Treatment Plants (WWTPs) recognized as the main contributors. Since conventional WWTPs were not originally designed to remove pharmaceutical residues, leading to the continuous discharge of these contaminants into surface waters. In response, the European Commission adopted the revised Urban Wastewater Treatment Directive (UWWTD) in late 2024, establishing minimum removal requirements for selected pharmaceuticals in municipal wastewater [2]. This directive mandates the implementation of an advanced (quaternary) treatment stage by 2045. Among the pharmaceuticals targeted for monitoring is hydrochlorothiazide (HCT), a commonly prescribed diuretic. In this context, the development of cost-effective and simplified analytical tools is essential to support WWTP operators in monitoring treatment efficiency and ensuring compliance with the new UWWTD standards. This work reports a paper-based electrochemical sensor for HCT analysis, employing a molecularly imprinted polymer (MIP) as the selective recognition element. A three-electrode electrochemical cell was fabricated by inkjet printing directly onto the paper substrate. The MIP film was then synthesized through electropolymerization on the working electrode's surface, that was previously modified with reduced graphene oxide (rGO). The developed sensor exhibited a good analytical performance and selective recognition of HCT. The sensor was successfully applied to tap water and WWTPs effluents, highlighting its promise as a simple, sustainable, and cost-effective solution for on-site HCT monitoring.

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